RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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Peptic Ulcer: The Importance of Films in Diagnosis[1]

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Seattle, Wash.

IT IS THE PURPOSE of this report to emphasize the important role played by roentgenologic films in identifying gastro-intestinal lesions, particularly gastric and duodenal ulcer. A high percentage of physicians share the opinion that the diagnosis of gastro-intestinal disease is based largely on fluoroscopic findings and that films, unless interpreted in the light of such findings, are usually meaningless. Fluoroscopy, by the simplicity of the apparatus and procedure and by its high diagnostic accuracy in proper hands, has discouraged interest in the potentialities of films. Emphasis on finding early lesions, particularly cancer, and on the potential dangers of excessive exposure to radiation is directing investigators to re-explore the possibility of using more films and less fluoroscopy.

The present situation is comparable to that of diseases of the chest and is stimulated by recent technical developments in the study of those diseases. Most lesions of the lungs are seen at fluoroscopy, but a certain percentage escape observation even by the experienced examiner. With routine use of films, even of the miniature variety, the number of pulmonary lesions overlooked has decreased. A similar situation holds for the gastro-intestinal tract, except for the use of miniature films, whose potentialities are now being explored. Most lesions can be seen at fluoroscopy, since most of them are large—in the order of a centimeter in diameter or more. It is in the smaller ones that films give the greatest aid. But even so, one is amazed at the apparent large size of certain lesions that escape detection under the fluoroscope. While this embarrassing situation is infrequent, it occurs often enough to cause one to speculate on the cause. Overwork and fatigue with the accompanying divided attention, failure to follow a set routine, and a combination of certain physical and physiologic phenomena, preventing clear images, are responsible for failures. Films play a valuable role in examination of the heavy patient in whom the fluoroscopic image is dim and will continue to play this role until amplification of the fluoroscopic image is a reality.

The gastro-intestinal tract is a pliable organ, capable of self motion. The contours are varied by contractions of the muscles and by extraneous influences, such as pressure on the abdominal wall. Since the appearance of the stomach and the duodenum varies from moment to moment, fluoroscopy is invaluable in studying the constantly changing pattern and to dif-

[1] From the Department of Radiology, University of Washington School of Medicine. Presented as part of a Symposium on Peptic Ulcer at the Thirty-fourth Annual Meeting of the Radiological Society of North America, San Francisco, Calif., Dec. 5–10, 1948.

ferentiate the normal from the abnormal. Witness, for example, the rigidity of the walls with the obliteration of peristalsis produced by neoplasm. However, with a few exceptions, somewhere in the cycle of motion or under the influence of pressure or with certain positions, there appear one or two anatomic patterns which impart the story. In most instances, these significant patterns, whether they be normal or abnormal, can be recorded on films, giving to these real diagnostic significance. If this statement is accepted, it follows that the primary purpose of fluoroscopy is to control the exposure of the roentgenograms.

If films are to play more important roles than they now do in most gastro-intestinal roentgen examinations, the diagnostic criteria must be based almost entirely on anatomic-pathologic changes. Anatomic-physiologic changes, such as those produced by peristalsis, tonus, and local contractions, while extremely helpful in some instances, can be recorded only by taking a series of several films with the patient's position unchanged or by observing the changing image under the fluoroscope. As helpful as peristalsis and tonus are in determining stiffening or pliability of the walls, certain limitations exist. Peristaltic waves either fail to appear when desired, are too shallow to be of much aid, or do not affect the zones of interest. The cardiac end of the stomach is an example of the latter.

With few exceptions, lesions which interfere with peristalsis produce anatomic abnormalities that can be detected by adequate technic. Some lesions, such as carcinoma, which are thought to produce their earliest signs by peristaltic paralysis, do not always do so. The abnormal variations in contours of the lumen or mucosal pattern produced by most ulcers must be demonstrated if one is to arrive at an unqualified diagnosis of ulcerous disease, even though peristaltic activity is altered. Proof that certain changes in physiology, such as "hyperperistalsis," "irritability," "delayed emptying," and "retention," are sufficient signs on which to base a diagnosis of ulcer is lacking. These signs are significant only if they are accompanied by demonstrable pathologic-anatomic changes. It is feasible and time-saving to locate lesions by observing the changes these abnormalities produce on the walls, seen in profile, and in the mucosal pattern. The identifying criteria for ulcers and their differentiation from spurious patterns have been described (1–4). There are, of course, findings of which one cannot be certain. Such situations are true of any diagnostic procedure, no matter how great the accuracy claimed for it. Supplementary examinations are essential for further evaluation. A detailed study of the physiologic variations often proves most helpful in these instances.

Representative films of various sections of the gastro-intestinal tract can be obtained with the filming-fluoroscope or "spot" machine. Best results are obtained by skilled operators who take routine exposures of various sections of the stomach and bulb during the course of the examination. By this method, lesions not seen at the fluoroscopic examination are detected. Those who record only abnormal shadows seen at fluoroscopy cannot realize the number of lesions overlooked, since the indications for surgical procedure, and even gastroscopic examination, are often dependent upon the results of a roentgen study.

Films, particularly spot films, are a most reliable medium for judging the quality of a fluoroscopic examination. Those who become expert in recording the significant images on spot films also perform creditable fluoroscopic examinations. Those who experience trouble in mastering the technic of using the filming-fluoroscope sometimes criticize the machine rather than themselves. This is a common human tendency. There is, I am sure, a direct relationship between the quality of the fluoroscopic examination and the quality of the films recorded.

The value of films in diagnosis and research cannot be overestimated. By re-

cording images in their nearly true form, by studying these permanent records at leisure, and by comparing the results with pathologic specimens, one becomes more and more proficient, not only in interpreting the films but also in observing significant changes at fluoroscopy. Permanent records are valuable to compare pathologic data and in following peptic ulcers during treatment, where one wishes to estimate the efficiency of medical management. Estimates as to the size of a crater from the fluoroscopic image do not always agree with the measurements on the films. Furthermore, the crater as it becomes smaller and smaller is lost at fluoroscopy before it is lost on the roentgenogram.

In closing, the following points are emphasized. Both fluoroscopy and films are essential parts of a good gastro-intestinal examination. Films properly made reveal enough data to allow a diagnosis in most instances, but such films cannot be obtained without fluoroscopic control. Significant images overlooked at fluoroscopic examination can be recorded on films; therefore routine films should be made of the various sections of the tract during the examination. It is obvious that objective evidence of a lesion is much more reassuring than subjective, not only to the radiologist but also the clinician who refers the patient. If the radiologist depends entirely or almost entirely upon fluoroscopy, the clinician is forced to view his patient through the eyes of the fluoroscopist and is denied the privilege of having objective data from which he can draw his own conclusions.

The confidence the clinician has in his radiologist is undermined by each lesion the latter fails to find. By reviewing the films which record the progress of the examination, both clinician and radiologist may find that the lesion occurred in a manner not possible to demonstrate with the technics in vogue. The clinician thus becomes more understanding of radiologic problems. Unfortunately, most errors can be traced to a break in routine, a fault which is much more evident from a review of films than of fluoroscopic notes.

To obtain representative films requires considerable skill and experience on the part of the radiologist, and deficiencies in technic are more obvious in one who uses the spot machine than in one whose sole reliance is on the fluoroscope. To keep up with expanding health programs, more thought will have to be given to the technic of examining the gastro-intestinal tract than it has received in the past, from the standpoint of increased accuracy and decreased radiation hazards to both the patient and the examiner.

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SUMARIO

Ulcera Péptica: Importancia de las Radiografías en el Diagnóstico

Para un buen examen gastrointestinal, resultan indispensables tanto la roentgenoscopia como las radiografías, y en particular las radiografías tomadas en el transcurso de la roentgenoscopia. Sin embargo, hay que hacer mayor hincapié en el papel desempeñado por las últimas, sobre todo en el diagnóstico de la úlcera gástrica y duodenal. Las radiografías debidamente obtenidas revelan suficientes datos para permitir el diagnóstico en la mayor parte de los casos, pero no pueden obtenerse sin comprobación roentgenoscópica. Una alteración importante que se pasa por alto en

la roentgenoscopia puede ser registrada en la radiografía, por cuya razon deben tomarse durante el examen radiografías corrientes de varios sectores del aparato gastrointestinal. Esos registros permanentes permiten estudio más detenido, comparación con los hallazgos patológicos y mejor apreciación de los efectos del tratamiento, facilitando además datos objetivos para el clínico que, de otro modo, sólo podría contemplar a su enfermo por los ojos del roentgenoscopista.

La obtención de radiografías adecuadas exige destreza y experiencia de parte del radiólogo, pues las deficiencias técnicas resaltan más en ellas que en el examen roentgenoscópico solo. A fin de mantenerse en ritmo con la expansión de las obras sanitarias, hay que prestar mayor consideración a la técnica del examen radiológico del aparato digestivo, desde el punto de vista tanto del aumento de la exactitud como de la disminución de los riesgos de la irradiación.

Place of Fluoroscopy in the Diagnosis of Peptic Ulcer[1]

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RUSSELL D. CARMAN, who, if not the father of roentgenoscopy in this country, is certainly the first active protagonist (Brown), stated in 1920, and iterated in the earlier edition of his book and papers: "I believe that the advantages of the screen in examination of the digestive tract can hardly be too strongly emphasized. Only by its use can exact information be obtained as to mobility and flexibility, the phenomena of peristalsis and antiperistalsis, the nature and permanence of irregularities of contour and effects of palpation, respiratory movement and varying positions. All changes can be seen at every instant, in the order of their succession, at any desired angle, and in these respects a few minutes of screening is equivalent to hundreds of plates." Plates were used mainly to record findings and only secondarily to check them. This tradition has been carried on and amplified, and the technic has been improved, by Carman's associates and successors, Drs. A. B. Moore, B. R. Kirklin, John D. Camp, and H. M. Weber.

It is comparatively recently that filming fluoroscopes or fluoroscopes with spot-film devices have been made available by the manufacturers of x-ray apparatus in this country (Templeton). Along with their availability, there has developed an intimation of controversy in x-ray diagnostic circles relative to the evaluation of the different methods of examination of the gastro-intestinal tract. Those who use the films taken during fluoroscopy as the main factor in diagnosis belittle those who depend primarily on the fluoroscopic observations and on films secondarily, and claim that the former method results in better detail and more accurate diagnosis.

It is my thesis that fluoroscopy and the few films necessary to record the findings are capable of extremely accurate and confirmable results when used by certain radiologists, *i.e.*, those trained by long experience and capable of substituting for the sharply focused macular vision used with intense light, the low intensity (retinal) rod vision necessary for viewing the screen image. This facility is an art requiring sharp visual acuity, mental alertness, and co-ordination far beyond that needed for mere observation of the varying densities of a photographic emulsion. It is not for those incapable of seeing the wealth of detail that can be revealed by the fluoroscopic screen and the proper manipulation of the patient and the shutters.

The fluoroscope itself should be as an old friend: well known, with few eccentricities. The manipulation should be an unconscious co-ordination of eyes, hands, and controls, such as only the familiarity of constant use can confer. The screen and tube carriage should float, move with little effort, and stay put when stationary. The shutter controls should obey the slightest motion of the hand—something lacking in the Belden cable control used in most of the present left-handed tilting fluoroscopes. Certainly, many of the European and late model American filming fluoroscopes, with their clumsy, cumbersome screen carriages, littered with levers, cassette holders, shifters, buttons, and now a photocell, with a tiny screen, are not conducive to relaxed subconscious manipulation. With all the mental and physical effort necessary in the manipulation of such apparatus, fluoroscopy becomes very casual, as the fluoroscopist must be busy taking films.

There is no question but that films

[1] Presented as part of a Symposium on Peptic Ulcer at the Thirty-fourth Annual Meeting of the Radiological Society of North America, San Francisco, Calif., Dec. 5–10, 1948.

should be taken of the organs under examination. There is also no question but that the filming fluoroscope is capable of taking these at the time of seeing the parts on the screen much more readily than taking them in a routine position. The question of dependence on the films thus made as a method of recording the fluoroscopic findings or as a major method of diagnosis is one for the individual examiner. Certainly there are radiologists who, because of an inherent inability to see well in the dark, should not depend on the fluoroscope in diagnosis, but should use it more or less for positioning, depending on the films produced for the final conclusion. All roentgenologists should test their visual acuity by methods advocated by Chamberlain and others.

It might be well to mention mechanical, psychological, and other factors which should be considered in making an adequate fluoroscopic examination. These are, in brief outline, the teachings of my preceptor, Dr. B. R. Kirklin, as I remember and apply them. In his paper before the Radiological Society of North America (1935), the technic of the examination is outlined in his lucid and striking manner.

In addition to the gross mechanical attributes of a "good" fluoroscope mentioned above, the type of tube and screen must be considered. A fine focal spot is essential. In spite of some who say otherwise, one can tell the difference in screen detail between a 1.5 mm. focal spot and a 3.0 mm. spot, this at the usual 12 to 14 inch distance of the tube from the table. At a distance of 20 inches or more, as advocated by Chamberlain, this difference would not be so evident. The screen should be as fast as possible without obvious graininess, producing good illumination, but with good contrast characteristics. Such a screen is the new Patterson type B-2.

The contrast medium to be used is important only in that it should be fluid enough to flow easily, and at the same time be sufficiently dense to obscure *on the screen* all bone and soft tissue detail, even in fairly thin layers. Flavored suspending agents usually produce too thick a mixture, and are still ineffective in disguising the taste of the barium sulfate. A drop of peppermint oil to a glass results in fewer objections to the mixture (Garland).

An important factor in fluoroscopy is the attitude of the patient under examination. For practically all, it is a new experience and nearly all are apprehensive, to say the least. Here the attitude of the personnel in the department is important. They should be cheerful, handle the patient as little as possible, and work toward putting him at ease. Most of the patients do not know how to relax, and must be told (Carman) to bend the head forward, allow the shoulders to relax, with the arms at the sides, and to let the abdomen sag. This procedure allows the stomach in all but those of the most hypersthenic habitus to come down below the costal margin, where all of it, except the fundus, can be palpated.

The question of dark adaptation before fluoroscopic examinations cannot be too greatly stressed. Chamberlain in his classic review of fluoroscopes and fluoroscopy in the Carman Lecture of 1941 has compiled data of great value. He outlines the scientific basis for prolonged dark adaptation before attempting fluoroscopy. Certainly, no one expecting to do adequate work will take less than thirty minutes to adapt his eyes, if he has been in bright sunlight, allowing for proportionally shorter times when adapting from a room with artificial illumination. The use of red goggles permits one to undertake such other duties as dictating letters, etc., even to driving a car. It must be understood that they do not shorten the time of dark adaption. Actually they should be supplemented by three to five minutes in a dark room to adapt the retinal cones to dim illumination.

After observation of the screen image, palpation is the next most important part of the examination. The co-ordination of the eye and the hand is most essential

and comes only with training and experience. It is quite obvious that only gross abnormalities are to be felt with the hand encased in a heavy lead glove. I do not hesitate to recommend the removal of that glove for direct palpation under fluoroscopic vision, provided the screen opening is kept small, the hand kept behind the barium shadow, and above all not placed in the direct beam. This advice is good, also, for those who depend on gloves for protection of the hand, for the 0.5 mm. lead equivalent in lead rubber does not give adequate protection in the direct beam of 80 to 90 kv. x-rays. One must remember that the black image of the glove seen on the screen is produced by two layers of the material, while the fingers are protected by only one.

The third most important factor in fluoroscopy is the proper use of the shutters. The screen opening should be as small as will give the maximum contrast between the barium-filled organ and the surrounding tissues. A set aperture cannot be used, for the illuminated portions of the screen should not exceed the shadow of the organ more than a centimeter or two. This requires constant adjustment of the shutters. A small shutter opening also affords considerable protection to the patient and to the examiner.

During the examination of the stomach, the first step should be the ingestion of a small amount of barium sulfate suspension, which should be manipulated to delineate the rugal folds of the entire stomach. Attention should be given to even slight variation from the normal configuration and it should be evaluated. The direct visualization of an ulcer crater is usually possible, if one is present. However, if there is a spastic incisura, shortening of the lesser curvature, or spasm of the gastric antrum without visualization of a crater, its presence should still be suspected and a re-examination should be made after administration of antispasmodics, if necessary, to confirm or rule it out (Carman). Sharply localized tenderness is also a suspicious finding.

After a thorough survey of the mucosal folds, the stomach should be distended with the barium sulfate suspension. The patient should then be turned in different positions for visualization of the walls of the stomach, especially the posterior wall along the length of the lesser curvature, as the examiner watches for the niche of a penetrating ulcer. The fundus can then be further examined by pressing the mixture upwards. (Supine and prone views of the fundus are also important.)

By the time this has been done, the pylorus has probably relaxed. It is at this point that proper relaxation of the patient is most important. All the manipulation possible will not force barium through the pylorus of a stomach with an atonic antrum. Reassurance of the patient, the mentioning of food, and gentle stroking of the antrum will increase its tone and further relax the pylorus. Peristalsis, helped by the manipulation, will then fill the cap. The type of manipulation is important. Pressing on the antrum, in an attempt to push the barium through the pylorus, results in compressing the cap against the liver and prevents the cap from filling. The proper procedure is to allow the antrum to fill by peristalsis; then, with just enough pressure to approximate the walls of the stomach, the cupped right hand is placed over the body of the stomach, at or just above the angle, and gentle downward pressure is produced in order to increase the intragastric pressure in the antrum. The cap then fills readily after one or two trials. Further increase of the pressure in the antrum may be obtained by pressure over it with the left thumb, which is then in position to obstruct the third portion of the duodenum, if necessary, to keep the cap filled. After the cap is filled, it is palpated and manipulated to disclose the folds of the mucosa. The variations of normal here are greater than those in the stomach, but departures from normal are equally important.

The importance of completely distending the cap cannot be stressed too much. In the absence of a previous surgical pro-

cedure in the region (especially involving the gallbladder), any persistent deformity of the cap represents a scar of a duodenal ulcer (Cole) and one in which active disease may be present. If the cap is not completely distended, apparent but not real deformity may be present and be quite persistent. The presence of a persistent fleck of barium surrounded by an areola of edematous tissue represents a penetrating ulcer crater on the anterior or posterior wall of the duodenum. A niche at the edge of the cap shadow, if it can be differentiated from a scar deformity or a pseudodiverticulum, also represents an active crater. These changes do not require films for their differentiation, but can be easily outlined on the screen. There is no question in my mind that they represent active disease—disease that can be confirmed by the surgeon or pathologist and fit the clinical picture of an active ulcer. However, active ulceration in the duodenum is not necessarily a process of ulcerous penetration. It can be an inflammatory infiltration of the duodenal wall without superficial ulcer or ulcers in the overlying mucosa. The only finding, either fluoroscopically or on film examination, is the persistent deformity. The determination of the activity of the process then depends on the clinical findings. One should remember that the clinician can help in differentiation and that the roentgenologist does not have to take the whole load on his shoulders, even if at times he is expected to do so.

The question of disappearance of the crater of a penetrating ulcer in the stomach as an indication of healing is an important one. Certainly ulcers under 10 mm. in diameter, located near or on the lesser curvature, can be considered to be healed when they disappear. Elsewhere in the stomach disappearance of an ulcer should be checked, not once, but several times before presuming that it is healed. Ulcers of any size on the greater curvature are so nearly always malignant that they should be treated as such after the initial diagnosis. The disappearance of an ulcer crater in the duodenum is presumptive evidence of healing, for the time being. It may, and probably will, recur after an interval, on the assumption of "once a duodenal ulcer, always a duodenal ulcer."

All these findings, seen so well under the fluoroscope and so easily recorded on films, are confirmable anatomically by the surgeon or pathologist. One questions the thesis of those whose main dependence is on films made during the screening of the patient, that the finer detail (especially the mucosa) produced on the films is of any particular significance. One might argue also that this method results in earlier diagnosis. However, in our office we have records, going back over many years, of patients with gastro-intestinal symptoms who persistently have shown no evidence of active disease. As a matter of fact, I remember only one patient who, examined at intervals over a period of about twenty years, finally was shown to have a duodenal ulcer at the age of sixty, and this after a period of about two years of symptoms considerably different from the previous ones.

Only very rarely does one find it necessary to re-examine the patient because of some suspicious findings on the films taken subsequent to the screen examination. One soon learns to anticipate possible film findings and thus check them beforehand.

In conclusion, the fluoroscope is the prime instrument in the x-ray diagnosis of diseases of the stomach and duodenum in the hands of roentgenologists capable of making full use of its facilities. Films for recording and checking the findings are necessary, but are of secondary importance. The demonstration of a penetrating ulcer in the stomach or duodenum indicates an active ulcer; disappearance of the crater is indicative of healing in duodenal ulcer, and probable healing of small ulcers on or near the lesser curvature of the stomach. Findings thus seen fluoroscopically and recorded on films can be confirmed anatomically, and it is not necessary to produce, by special proce-

dures during the examination, films on which prime dependence for the diagnosis is placed.

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SUMARIO

Puesto de la Roentgenoscopia en el Diagnóstico de la Ulcera Péptica

El roentgenoscopio es el instrumento primordial para el diagnóstico roentgenológico de las enfermedades del estómago y el duodeno en manos del radiólogo capaz de usar plenamente sus recursos. Exige, sin embargo, pronunciada agudeza visual, viveza mental, y coordinación muy superior a la necesaria para la mera observación de los distintos espesores en la película roentgenológica. Las radiografías dedicadas a registrar y comprobar los hallazgos son necesarias, pero revisten importancia secundaria.

La observación de una úlcera penetrante en el estómago o duodeno indica úlcera activa; la desaparición del cráter denota cicatrización en la úlcera duodenal y probable cicatrización en las ulcerillas de, o cerca de, la curvatura menor del estómago. Los signos así observados roentgenoscópicamente y registrados en las radiografías pueden ser confirmados anatómicamente, sin que sea necesario producir, por medio de procedimientos especiales durante el examen, radiografías en las que se base principalmente el diagnóstico.

Physical Problems of Fluoroscopy and Spot-Film Radiography[1]

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THE PHYSICAL problems of fluoroscopy and spot-film radiography may be divided into two principal categories: (*a*) those concerned with the radiation hazards to which the patient and radiologist are exposed during the performance of the procedures and (*b*) those concerned with the poor visibility which prevails during any fluoroscopic examination and especially during the fluoroscopic study of such heavy structures as the abdomen.

RADIATION HAZARDS

The effects of x-radiation on biological tissues are generally deleterious, and it is therefore important that the radiation to which the patient is exposed during gastro-intestinal study be maintained at a low value. This requires that the study be carried out under conditions in which the field of vision is restricted by the fluoroscopic shutters to the smallest possible size consistent with an adequate appreciation of the anatomical relationships under study and in which the time of exposure is reduced to the shortest possible interval consistent with a complete examination. Although the biophysicists who recently have expressed so much concern over the delivery of even minute quantities of x-radiation to the body are possibly unnecessarily apprehensive, there can be little doubt that fluoroscopic examinations in which the shutters are opened to give an aperture of the order of 200 square inches for periods of ten and fifteen minutes should be condemned. Unfortunately there are a few radiologists, and many more internists whose offices are equipped with fluoroscopic apparatus, who regularly persist in conducting their fluoroscopic procedures in just such a manner. It is

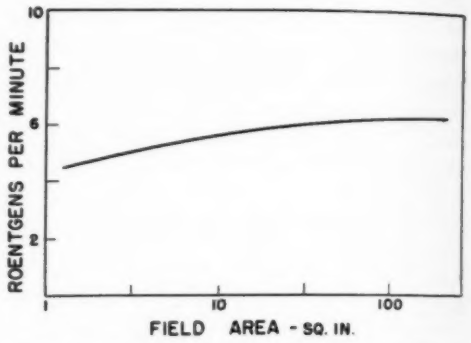

Fig. 1. Effect of field size on the roentgen dosage received by the incident skin surface of a patient during fluoroscopy. Conditions of exposure: tube potential, 85 kv.p.; tube current, 4 ma.; filter, 3 mm. Al; target-table top distance, 18 inches; phantom, 20 cm. of masonite tempered presdwood; field size measured at fluoroscopic screen; roentgen measurements include back-scatter.

therefore hoped that before long the screens with which conventional fluoroscopes are equipped will be reduced in size, either by convention or by regulation, to dimensions consideraly smaller than the 12 × 16 inches now provided.

Experience gained at the University of Chicago Clinics and the Johns Hopkins Hospital, where fluoroscopic screens of the order of 30 to 50 square inches have been in regular service for periods of several years, indicates that such small screens constitute no clinical problem in the examination of any anatomical structure. The small field sizes imposed by these screens have done much to reduce the radiation exposure of the patients who have been examined. This is well shown in Figure 1, where the dosage in roentgens, including back-scatter, received at the incident surface of a phantom of tempered masonite presdwood, 20 cm. in thickness, is plotted as a function of the field of observation on

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the fluoroscopic screen. The measurements were made with a fluoroscope operating at 85 kv.p. and 4 ma., with a filter of 3 mm. of aluminum and with a target-table top distance of 18 inches. It will be observed that the dosage becomes greater as the field size increases. This rise in dosage, however, does not indicate the entire radiation hazard. When the field of observation is small, the total length of time during which a *particular* area is exposed during an examination is likely to be considerably shorter than when the field is large, since in the latter case there will be considerable overlapping of the fields of observation from one moment to the next.

The long periods of fluoroscopy which some physicians require for examination of the alimentary tract can also constitute a serious radiation problem. It may be argued by some that prolonged fluoroscopy is frequently necessary to perform a *complete* examination. This stand, however, does not seem to be justified either by practical or experimental observations. Although there have been no serious studies on the psychological aspects of fluoroscopic vision, preliminary investigations which we have undertaken in this field indicate that almost all of the intelligence recorded on a fluoroscopic screen is appreciated by the observer within a few seconds after the image has appeared on the screen. Long periods of further scrutiny are usually of little value in determining additional diagnostic information. While the speed of intelligence-appreciation by an observer depends to a great extent on his experience, there seems to be little reason why the great majority of gastro-intestinal examinations need be prolonged beyond a period of five minutes of actual fluoroscopy for the average radiologist.

Such a period of fluoroscopy, when performed by a fluoroscope operating at 85 kv.p. and 4 ma., with a target-table top distance of 18 inches and a filter of 3 mm. of aluminum, with a field size sufficient to produce a screen image 40 square inches in area, will result in the delivery of a total of 30 r, including back-scatter, to the skin of a patient 20 cm. in thickness. The exposure to which any particular area of the skin is subjected will, of course, be smaller than this total value. The exposure does not seem excessive.

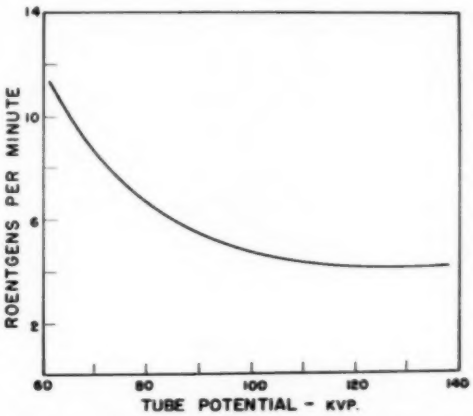

Fig. 2. Effect of x-ray tube potential on the roentgen dosage received by the incident skin surface of a patient during fluoroscopy. Conditions of exposure: tube current varied to maintain screen brightness constant at various tube potentials; field size 40 square inches; other conditions as given for Figure 1.

The size of the field of observation and the time taken for the performance of an examination do not constitute the only factors which control the radiation dosage during fluoroscopy. The kilovoltage applied to the roentgen tube, the target-table top distance, and the filtration in the roentgen beam also influence the quantity of radiation to which a patient is subjected. In Figure 2 is shown the dosage, including back-scatter, delivered to a tempered masonite phantom, 20 cm. in thickness, during fluoroscopy with a roentgen generator operating at various tube potentials. The data were obtained under conditions in which the tube current was varied so as to yield a screen brightness that remained constant throughout the range of kilovoltage studied (at 85 kv.p. the tube current was 4.0 ma.). The roentgen beam was filtered with 3 mm. of aluminum, the target-table top distance was 18 inches, and the field of observation was 40 square inches on the screen. It will be observed that for a given screen brightness, the ex-

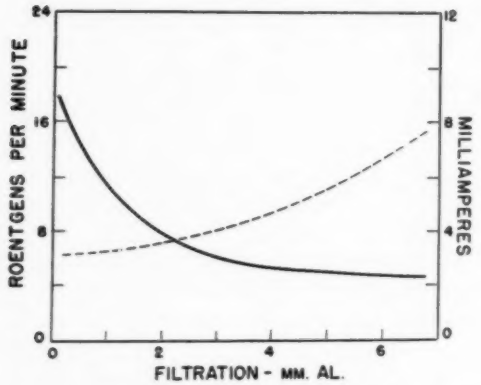

Fig. 3. Effect of aluminum filtration on the roentgen dosage received by the incident skin surface of a patient during fluoroscopy. Conditions of exposure: tube current varied to maintain screen brightness constant at various filter thicknesses; field size, 40 square inches; other conditions as given for Figure 1.

posure received by a patient diminishes as the tube potential is raised until a voltage of about 130 kv.p. is reached. Thereafter, there is a slight rise in the dosage value. From this, it would appear that fluoroscopy should be performed at tube potentials higher than those now used. However, it will be noted that the dosage conditions at 85 to 100 kv.p. are little less satisfactory than at 130 kv.p., and there seems to be no great need, therefore, for higher kilovoltages than those now generally employed from the standpoint of the radiation hazard involved.

The diminished dosage that occurs when the tube potential is increased is caused by changes in the spectral distribution of the radiation projected through the patient. When the potential rises, the fraction of the radiation which is composed of easily absorbed long-wave-length components diminishes and accordingly the dosage rate decreases. One should therefore expect that filtration in the roentgen beam might also affect the amount of radiation delivered to a patient during fluoroscopy. The magnitude of this effect is shown graphically in Figure 3, where the roentgen dosage, including back-scatter, delivered to a tempered masonite phantom, 20 cm. in thickness, when fluoroscoped by a roentgen generator operating at 85 kv.p., is plotted against thickness of aluminum filtration placed in the beam. These measurements were made with a roentgen tube having an inherent filtration of 0.7 mm. of aluminum, and operating at tube currents which yielded a screen brightness that remained constant through the range of filter thickness studied (at 3 mm. of aluminum the tube current was 4.0 ma.). The target-table top distance was 18 inches and the field of observation was 40 square inches at the screen.

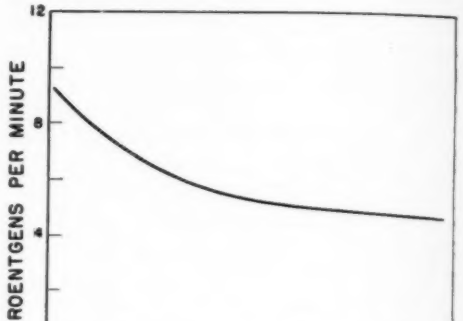

Fig. 4. Effect of target-table top distance on the roentgen exposure delivered to the incident skin surface of a patient during fluoroscopy. Conditions of exposure: tube current varied to maintain screen brightness constant at various target-table top distances; field size, 40 square inches; other conditions as given for Figure 1.

It will be observed that increases in filter thickness markedly decrease the incident radiation dosage received by the patient. Furthermore, this effect is obtained at very little cost in extra milliamperage needed to maintain the screen at its original brightness (see dotted curve in Fig. 3). It therefore appears that more filtration than that customarily used in the roentgen beam during fluoroscopy is desirable; indeed, filters of 2 to 4 mm. in thickness should provide very real reductions in the quantity of radiation to which patients are subjected during fluoroscopy.

In recent years, considerable attention has been given to the effect of increased target-table top distances in decreasing the radiation exposure of a patient (1).

This effect, however, is not as great as might be anticipated. In Figure 4, the roentgen dosage, including back-scatter, delivered to a tempered masonite phantom, 20 cm. in thickness, when fluoroscoped with a roentgen generator operating at 85 kv.p., and filtered with 3 mm. of aluminum, is plotted as a function of the target-table top distance. These data were obtained with the roentgen tube operating at currents such that the brightness of the fluoroscopic screen remained constant throughout the ranges of target-table top distances studied. It will be observed that, although the roentgen dosage rate diminishes as the target-table top distance increases, the change is not great for values over 15 inches; for example, the dosage rate is only down 16 per cent when the distance is increased from 15 to 20 inches.

The effect of spot-film radiography on the quantity of radiation delivered to a patient during fluoroscopy has been of considerable concern to many radiologists in recent years. There seems, however, to be little basis for this apprehension. The quantity of radiation delivered at each spot-film exposure will, of course, depend on the equipment on which the films are made, but with conventional equipment the exposures may be expected to be of the order of 20 to 50 ma.-seconds. If a series of six films is made (possibly the number needed for the complete study of an average individual), 120 to 300 ma.-seconds will constitute the necessary exposure for the entire set of films. However, if the patient is fluoroscoped for a period of five minutes at a tube current of let us say 4.0 ma., the total fluoroscopic exposure will approach 1,200 ma.-seconds. Thus, the set of spot-films will constitute a roentgen exposure of only 10 to 25 per cent of that received during fluoroscopy. Such an extra exposure can hardly be thought deleterious in view of our knowledge of the relatively large percentage changes in radiation exposure needed to produce a change in biological reaction.

Although spot-film radiography in general appears to be a safe procedure from the standpoint of radiation hazard, there is one practice that is commonly employed in the method that has considerable potential danger; that is the practice of using field-limiting compression devices when one is seeking mucosal relief views of the stomach or duodenum. These devices are normally located between the patient and screen and, when in place, permit the fluoroscopist to examine the patient with good visibility even though the shutters of the fluoroscope may be wide open. Indeed, unless great care is exercised by the radiologist, films will be made under this undesirable condition more often than not. If adequate protection is to be maintained, the devices that are used for compression should not be devices that also limit the field of fluoroscopic vision. Furthermore,

Fig. 5. Spot-film fluoroscope constructed in the radiology model shop of the Johns Hopkins Hospital. Unit includes fine-focus rotating-anode tube, moving grid, automatic photoelectric timer, and compression apparatus independent of field-limiting devices. Table-tilting mechanism is electrically activated by a switch on the front of the screen to facilitate operation of the table ith sick patients. A low-intensity pilot light at the top of the screen has been added to throw light on barium glasses when they are handed to patients. Light comes on when red light of room is lighted.

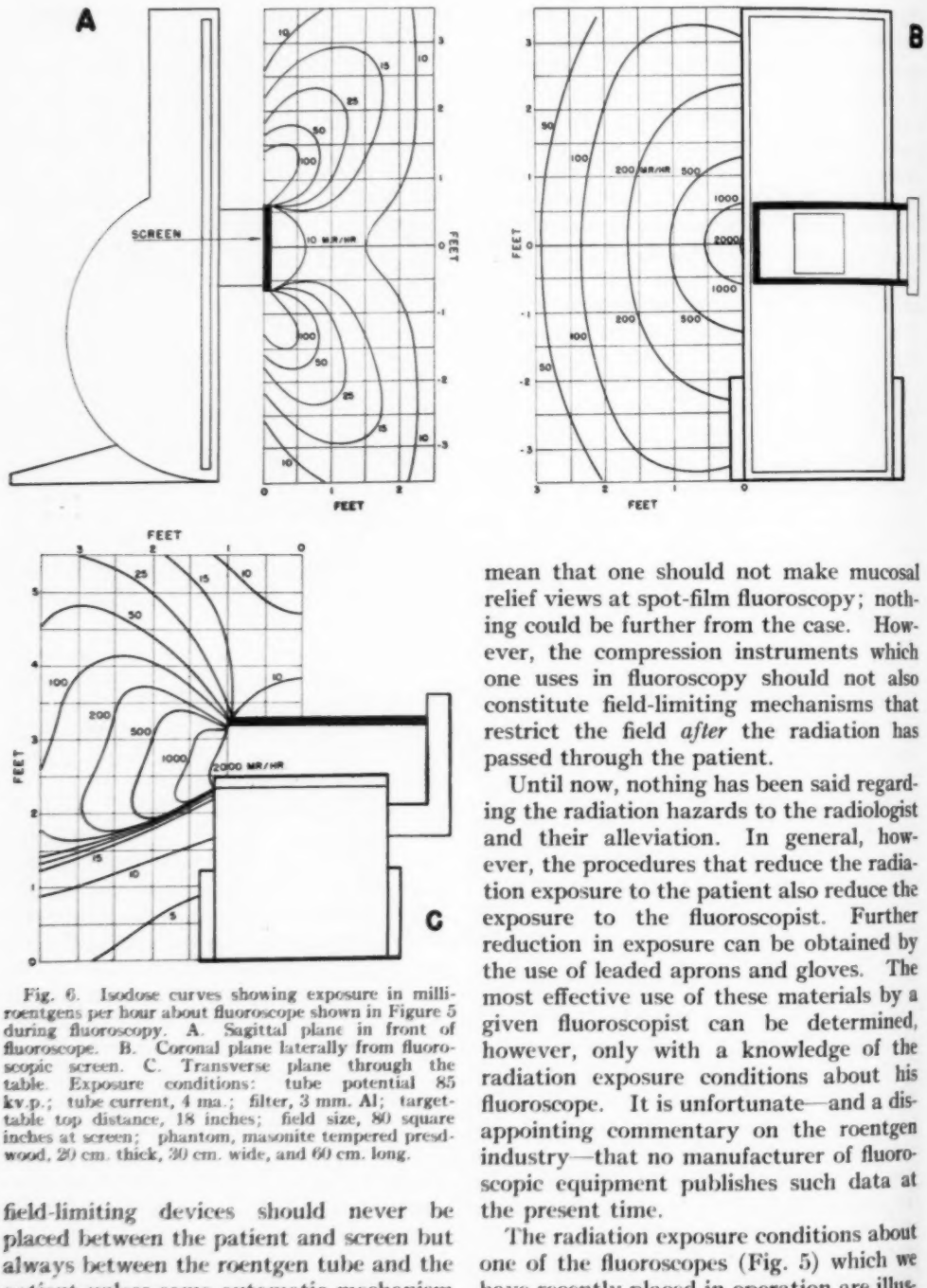

Fig. 6. Isodose curves showing exposure in milliroentgens per hour about fluoroscope shown in Figure 5 during fluoroscopy. A. Sagittal plane in front of fluoroscope. B. Coronal plane laterally from fluoroscopic screen. C. Transverse plane through the table. Exposure conditions: tube potential 85 kv.p.; tube current, 4 ma.; filter, 3 mm. Al; target-table top distance, 18 inches; field size, 80 square inches at screen; phantom, masonite tempered presdwood, 20 cm. thick, 30 cm. wide, and 60 cm. long.

field-limiting devices should never be placed between the patient and screen but always between the roentgen tube and the patient unless some automatic mechanism is provided to limit the shutter opening when the device is in place. This does not mean that one should not make mucosal relief views at spot-film fluoroscopy; nothing could be further from the case. However, the compression instruments which one uses in fluoroscopy should not also constitute field-limiting mechanisms that restrict the field *after* the radiation has passed through the patient.

Until now, nothing has been said regarding the radiation hazards to the radiologist and their alleviation. In general, however, the procedures that reduce the radiation exposure to the patient also reduce the exposure to the fluoroscopist. Further reduction in exposure can be obtained by the use of leaded aprons and gloves. The most effective use of these materials by a given fluoroscopist can be determined, however, only with a knowledge of the radiation exposure conditions about his fluoroscope. It is unfortunate—and a disappointing commentary on the roentgen industry—that no manufacturer of fluoroscopic equipment publishes such data at the present time.

The radiation exposure conditions about one of the fluoroscopes (Fig. 5) which we have recently placed in operation are illustrated in Figure 6A–C. This fluoroscope is basically a Westinghouse Duoflex model

that has been altered in our laboratory shops to permit the same flexibility in spot-film radiography as is provided by the fluoroscope designed by Hodges and described by Templeton (2). The maximum field of vision at the screen is 80 square inches. All of the data presented in Figure 6 were obtained with a tempered masonite presdwood phantom 20 cm. in thickness, 30 cm. wide, and 60 cm. long. The fluoroscopic beam was provided by a generator operating at 85 kv.p. and 4.0 ma. The beam had a filter of 3 mm. of aluminum, the target-table top distance was 18 inches, and the observational field at the screen was 80 square inches. Figure 6A shows the exposure conditions in a sagittal plane in front of the fluoroscopic screen; the data in Figure 6B indicate the exposure conditions in a coronal plane laterally from the fluoroscopic screen, while those in Figure 6C are in a transverse plane through the table. It will be observed that the danger areas extend (*a*) laterally on either side of the fluoroscopic screen in a direction where the radiologist stands while examining the patient in the recumbent position and (*b*) anteriorly above and below the fluoroscopic screen where the radiologist sits when examining the patient in the vertical position. Almost all of the radiation exposure occurring in these two locations is composed of scattered radiation arising in the patient. The lead glass covering the fluoroscopic screen appears to prevent effectively the transmission of significant quantities of direct radiation.

Leaded aprons are fairly efficient in absorbing the scattered radiation to which the radiologist is exposed. One commercial apron having a lead equivalence of 0.5 mm. transmitted only 1 per cent of the scattered radiation incident upon it under the conditions which were employed for the collection of the data illustrated in Figure 6. It appears, therefore, that such an apron will provide sufficient protection to enable the radiologist to conduct fluoroscopic examinations for considerable periods each day without exceeding an exposure of 0.1 r at any location about the fluoroscope. However, it must be pointed out that present-day aprons do not always cover the body in the regions where maximum exposure is encountered. For example, in Figure 6A, it will be seen that the area of greatest danger occurs immediately below the fluoroscopic screen, where the shoulders and neck of the fluoroscopist, unprotected by conventional aprons, are located. It therefore seems desirable that additional protective measures, such as leaded rubber curtains, be placed about the bottom of the fluoroscopic screen to insure the absorption of the high-intensity radiation which exists at this location.

Before leaving the problems of radiation protection in fluoroscopy, it may be well to say a word or two regarding the hazards of placing the hand in the so-called direct roentgen beam between the patient and the fluoroscopic screen. Measurements of the radiation exposure existing within a 2-ply Liberty Dressing Company glove when placed in the center of the irradiated field in front of a 20-cm. presdwood phantom with the fluoroscope operating at 85 kv.p. and 4.0 ma., with 3 mm. of aluminum filtration, and with an 18-inch target-table top distance, indicate that 0.05 r per hour may be expected at this location. It therefore appears that the hand of the operator, when protected by such a glove, may be placed in the direct beam for short periods. In this connection, it is regrettable that present-day gloves do not cover more of the forearm. It is apparent from Figure 6A that, when the protected hand is placed in the direct roentgen beam, the unprotected forearm is exposed to undesirably high radiation intensities scattered outside the direct beam.

FLUOROSCOPIC VISIBILITY

The poor visibility which prevails during fluoroscopy is well known. Its cause is not to be found in any deficiencies of the fluoroscopic screen or even within the human visual mechanism, but instead in the relatively large statistical fluctuations which exist from moment to moment in the intensity of the fluoroscopic beam.

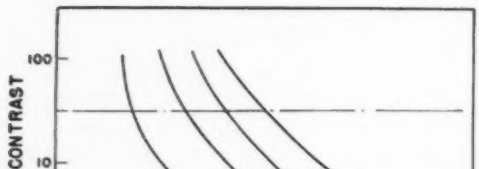

Fig. 7. Visual performance curves in which per cent threshold contrast is plotted as a function of minimum perceptible image diameter during fluoroscopy. A. 10-cm. presdwood phantom. B. 20-cm. presdwood phantom. C. 30-cm. presdwood phantom. Exposure conditions: tube potential, 85 kv.p.; tube current, 4 ma.; filter, 3 mm. Al.; target-table top distance, 18 inches; screen, Patterson B-2; field size, 80 square inches. Curve D indicates visual performance during radiography with Patterson par speed screens and Eastman blue brand film.

These fluctuations could be reduced and visibility improved by increasing the beam intensity several hundred times. However, such a solution to the problem is obviously impractical. Another solution is the development of an electronic screen intensifier by which the brightness of the fluoroscopic screen could be increased and the fluctuations in the screen's light output reduced to at least some extent (3). Although such screen intensifiers are now in the experimental stage, practical devices will probably not be available for a few years, and it appears that for some time to come poor fluoroscopic visibility will continue to be the rule.

Fluoroscopic visibility is a function of the sizes of the images under observation and of the contrast they exhibit with their surrounding fields. This is well shown in Figure 7, where the smallest image size which may be perceived at fluoroscopy is plotted as a function of image contrast for conditions where the roentgen generator is operating at 85 kv.p. and 4.0 ma., with a 3-mm. aluminum filter, an 18-inch target-table top distance, and with a Patterson type B-2 screen. Curves A, B, and C represent conditions respectively when the structure under observation is equivalent to 10, 20, and 30 cm. of masonite presdwood in thickness. Images of sizes and contrasts that fall above and to the right of each curve are readily seen; those that fall below and to the left of each curve are invisible. The range of contrast between the dotted lines is the range normally encountered in fluoroscopic practice.

The threshold visibility data for radiography are depicted in curve D of Figure 7. It will be noted that visual performance at radiography is markedly better than that at fluoroscopy. For example, an image of 30 per cent contrast must be fifteen times larger to be seen at abdominal fluoroscopy (equal to 20 cm. of presdwood) than at radiography.

In the absence of screen intensification systems, radiologists long ago began using spot-film radiography for better visualization of the gastro-intestinal tract. Although spot-film technics have been widely used, it is rather surprising that they have not received an overwhelmingly enthusiastic reception in view of the data illustrated in Figure 7. One reason for this may be the radiation hazard that is involved. However, as we have pointed out above, the procedure involves no serious radiation hazard. The major reason why spot-film technics are not universally used is probably the poor quality of the films that may be obtained with conventional fluoroscopic equipment at the present time. The performance of almost all of these devices falls far short of curve D in Figure 7. This is due, first, to the large focal spot sizes that are often used for spot-film radiography and which produce blurring of the images; second, to the difficulty of frequent and correct adjustment of the exposure factors of the x-ray machine as the examination proceeds so that properly exposed films will be consistently produced. By and large, gastro-intestinal spot-films are usually the most poorly exposed films made in a department of radiology, since it is almost impossible for the fluoroscopist to gauge, time after time,

the proper exposure factors as the patient is placed first in one position and then in another.

Fortunately, the technical problems of spot-film radiography that have just been cited are being solved. Fluoroscopes with fine-focus rotating-anode tubes are now generally available, and fluoroscopes with automatic phototiming on their spot-film devices are being produced by several manufacturers. Spot-film radiography probably constitutes the most valuable of all applications of automatic photoelectric timers. From the moment the switch of the fluoroscope is turned on, these timers permit the fluoroscopist to forget entirely the technical workings of his equipment and to devote his undivided attention to the clinical problems of his patient.

Another factor which frequently leads to poor quality in spot-films is the failure to use a grid when the exposure is made. As we shall see shortly, the use of a grid in conventional fluoroscopy is not so important, but when films are to be obtained, the contrast will be undesirably low unless a grid is employed. Some radiologists object to the grid lines that occur on the films made with conventional stationary grids. It appears likely that moving grids may become available on spot-film equipment before long and eliminate this difficulty. Such a grid has been installed in the fluoroscope shown in Figure 5.

Although fine-focus x-ray tubes and stationary grids have found their greatest usefulness in spot-film radiography, they have been advocated by some for conventional fluoroscopy. The comparative merits of fine-focus tubes over coarse-focus tubes are illustrated in Figure 8, where the smallest image which may be perceived at fluoroscopy is plotted as a function of image contrast. The solid curves are identical with those shown in Figure 7 and represent conditions where disks of essentially perfect sharpness are viewed on fields of varying contrast under the fluoroscopic conditions specified for Figure 7. The dotted curves, on the other hand, represent conditions in which the disks are placed in such a position between the x-ray tube and the fluoroscopic screen that the geometric unsharpness at the image boundaries on the screen is 1 mm. (the unsharpness that would be produced by objects examined fluoroscopically with a tube having a 5-mm. focal spot and placed 20 inches in front of the x-ray tube and 4 inches behind the screen).

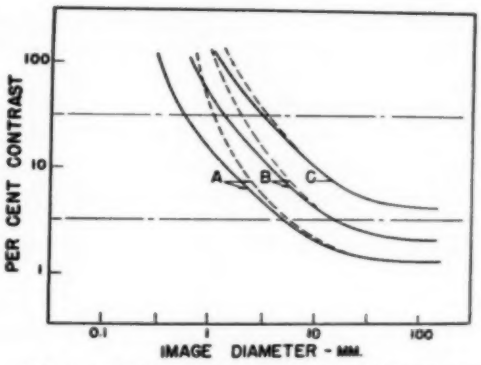

Fig. 8. Visual performance curves in which per cent threshold contrast is plotted as a function of minimum perceptible image diameter. Solid curves are identical with those in Figure 7. Dotted curves represent conditions in which the images on the screen are produced by objects placed 20 inches in front of the x-ray tube and 4 inches behind the fluoroscopic screen and examined fluoroscopically with a tube having a focal spot 5 mm. in diameter.

It will be observed that some improvement in vision occurs when the unsharpness caused by the large focal spot is removed. The effect is greatest when the structure under examination is thinnest (*i. e.*, when the screen is brightest). It therefore seems well worth while to use fine-focus tubes for fluoroscopy.

It is well known that grids do not seem as advantageous in fluoroscopy as in radiography. The reason for this may be found in the fact that, although a grid improves the contrast of an image, it also decreases its brightness. The net result, therefore, is not the spectacular change that is seen in radiography. However, it has recently been shown (3) that the improvement in visibility due to the increased contrast provided by a grid is greater than the loss

of visibility due to the decreased screen brightness, and there is therefore no doubt that grids are generally desirable for conventional fluoroscopy.[2]

[2] The relationship between the size of the smallest image that can be perceived at fluoroscopy, the contrast of the image and the brightness of the fluoroscopic screen may be expressed by the general equation

$$d = \frac{k}{CB^{1/2}} \tag{1}$$

where d is the image diameter, C is the image contrast, B is the screen brightness, and k is a constant.

Also, the contrast of an image may be defined as

$$C = \frac{\Delta B}{B} \tag{2}$$

where ΔB is the difference in brightness between the image and its surrounding field.

Now, in fluoroscopy, if it were possible to prevent all scattered radiation from reaching the screen, let us say by a perfect grid, then the contrast of the image would be

$$C = \frac{\Delta B_p}{B_p} \tag{3}$$

where the subscript p indicates that the light emitted from the screen is due entirely to primary x-radiation. If no grid were used, the contrast value would be

$$C_t = \frac{\Delta B_p}{B_t} \tag{4}$$

where the subscript t indicates that the light emitted from the screen is produced by the total radiation products, primary and secondary, transmitted from the patient.

It is evident from equations (1), (2), and (3) that the smallest perceptible image that may be seen when a perfect grid is used is given by the equation

$$d_p = \frac{kB_p^{1/2}}{\Delta B_p} \tag{5}$$

Also, when a grid is not used,

$$d_t = \frac{kB_t^{1/2}}{\Delta B_p} \tag{6}$$

When equation (5) is divided by equation (6)

$$\frac{d_p}{d_t} = \left(\frac{B_p}{B_t}\right)^{1/2} \tag{7}$$

Since B_p is smaller than B_t, equation (7) indicates that d_p is smaller than d_t; that is, smaller images may be seen when a grid is employed at fluoroscopy than when it is not used. The improvement in visibility is not proportional, however, to the ratio of the screen brightnesses with and without a grid, as it is for radiography, but only proportional to the square root of the ratio. Thus, the usefulness of a grid during fluoroscopy is not so apparent as in radiography.

SUMMARY

The discussion of the physical problems of fluoroscopy and spot-film radiography that has been developed in the foregoing pages appears to indicate that the radiation hazards attendant on these procedures may be minimized (*a*) by maintaining the fields of fluoroscopic observation as small as possible, (*b*) by keeping the time of fluoroscopy short, (*c*) by providing 2 to 4 mm. of aluminum filtration in the x-ray beam, and (*d*) by plotting the exposure conditions that exist about one's fluoroscope and introducing such extra protective measures beyond those provided by apron and gloves as may be necessary. In addition, the hazards will be somewhat further reduced by increasing the target-table top distance and increasing the x-ray tube potentials to levels of 85 to 100 kv.p. No significant radiation hazard is introduced by the employment of spot-film radiographic technics in routine fluoroscopic practice.

The problems of poor visibility that exist during fluoroscopy may be solved by the use of spot-film radiography. Full advantage of this procedure, however, can be taken only when a fine-focus rotating-anode x-ray tube, a stationary grid, and an automatic phototimer are used. A grid and a fine-focus x-ray tube also benefit conventional fluoroscopy to an extent sufficient to merit their general use in this field.

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SUMARIO

Problemas Físicos de la Roentgenoscopia y la Radiografía Instantánea

El estudio de los problemas físicos planteados por la fluoroscopia y la radiografía instantánea parece indicar que pueden reducirse a un mínimo los riesgos de la irradiación: (*a*) manteniendo los campos de observación roentgenoscópica lo más pequeños posible; (*b*) abreviando la duración de la roentgenoscopia, (*c*) facilitando una filtración del haz de rayos X por 2 a 4 mm. de aluminio, y (*d*) delineando las condiciones de exposición que existen alrededor del roentgenoscopio e introduciendo las providencias extraordinarias de protección que parezcan necesarias, aparte de las ofrecidas por el delantal y los guantes. Los riesgos serán algo atenuados aumentando la distancia desde la porción superior de la mesa al blanco e igualmente los potenciales de los tubos de rayos X a cifras de 85 a 100 kv.p. El empleo de la radiografía instantánea en el curso de la roentgenoscopia no agrega mayor riesgo a la irradiación.

Los problemas creados por la mala visibilidad durante la fluoroscopia pueden ser resueltos con el empleo de la radiografía instantánea, pero para aprovechar plenamente la misma hay que utilizar un tubo de rayos X de ánodo rotatorio y foco fino, una rejilla estacionaria y un fotocronógrafo automático. Una rejilla y un tubo de rayos X de foco fino también benefician la roentgenoscopia corriente lo suficiente para justificar su empleo general en dicho procedimiento.

Gastroscopy in the Evaluation of Patients with Peptic Ulcer[1]

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THE OBJECT OF this paper is to discuss the value and limitations of gastroscopy as a diagnostic aid and as a guide to the efficacy of therapy in patients with duodenal, gastric, and stomal ulcers.

A gastroscopic study may readily be made in fasting patients on an ambulatory basis, with local anesthesia of the pharynx. While the patient lies on his left side, the instrument, which is flexible and covered with rubber in the portion which lies in the lower esophagus and stomach, is inserted. A prism at the distal end enables various areas of the gastric mucosa to be seen at right angles to the axis of the instrument. A series of convex lenses allows a clear image to be maintained if the flexible portion is deviated not more than 30° at any single point. During the procedure the stomach is inflated with air through a passage inside the instrument.

Upon the initial insertion of the gastroscope, the pylorus should be sought as a major landmark and should be seen in 90 per cent of undistorted stomachs (1). A second landmark, the incisura angularis, is an arch-like fold on the lesser curvature which separates the antrum from the body of the stomach. This fold, caused simply by the angulation of the stomach, corresponds roughly to the incisura demonstrated radiologically. Deep peristaltic waves may be seen to cross the antrum associated with contractions of the pylorus.

Three zones of the stomach are not visible gastroscopically: the posterior wall on which the instrument lies, the lowermost lesser curvature behind the incisura angularis, and the cardiac portion of the stomach which domes above the entrance of the esophagus. No portion of the esophagus can be seen gastroscopically. Radiographic studies made by Ould and Dailey (2) demonstrated that the gastroscope clings closely to the posterior wall near the lesser curvature. This is the reason why it is frequently difficult or impossible to visualize lesions of the posterior wall, since the focal distance of the lens of the instrument is approximately 1.5 cm.

The contraindications to gastroscopy include esophageal diverticula, varices, and neoplasms; cardiospasm; aortic aneurysm; severe deformities of the thoracic spine; gastric tumors which encroach upon the cardia. Age is not a contraindication, our oldest patient being eighty-six years of age. Nearly all patients are entirely cooperative when the procedure is explained to them and they are assured of the absence of pain.

Several studies have been made which compare the accuracy and relative value of competent radiographic and gastroscopic examination of the stomach; that of Benedict (3) is one of the most recent, objective, and comprehensive appraisals. Since a major gain from gastroscopy is the evaluation of radiographic findings, it is evident that an appreciation of the value and limitations of each method of examination is desirable. Only on rare occasions is gastroscopy performed prior to barium examination, and it is the radiologist, therefore, who informs the gastroscopist as to the sites of various lesions and where the major portion of the examining time should be spent. Gastroscopy and radiography of the stomach are methods which nicely complement each other, the former enabling one to see large areas of mucosa in

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detail and the latter to discover abnormalities of contour, pliability, or peristalsis, and to identify lesions in areas inaccessible to the gastroscope.

DUODENAL ULCER

In our experience gastritis associated with uncomplicated duodenal ulcer is not common, although Christiansen (4) reported an incidence of 61.4 per cent in 70 patients. In our series of 107 patients with duodenal ulcer the gastric mucosa was entirely normal in 82 (Table I). An additional 18 patients displayed an engorged hyperemic mucosa with soft enlarged succulent rugae. This is considered to be a purely physiologic change associated with the gastric hypersecretion so common in these patients. Wolf and Wolff (5) have noted this hyperfunctioning mucosa by observations through a gastrostomy stoma. Their subject was without gastrointestinal disease. Emotions such as resentment and drugs such as alcohol or histamine produced a hyperemic edematous mucosa which seems identical in appearance with the hyperfunctioning mucosa noted in our patients with duodenal ulcer. In this way, a gastritis is simulated but is obviously not present, since the hyperemia is transient, there is no thick adherent mucus, and the rugae are simply edematous with no evidence of gastritic infiltration. If such a hyperfunctioning mucosa occurs in patients with duodenal ulcer, and gastrectomy is contemplated, an especially high resection is indicated. In posterior penetrating duodenal ulcers, the pylorus may be displaced posteriorly, while with obstruction, minimal inflammatory changes may be present, apparently due to the retained acid secretion.

TABLE I: APPEARANCE OF GASTRIC MUCOSA IN 107 PATIENTS WITH DUODENAL ULCER

Normal gastric mucosa	82*
Hyperfunctioning mucosa	18
Superficial gastritis	2
Hypertrophic gastritis	1
Atrophic gastritis	1
Mucosal hemorrhages	1
Gastric ulcer, benign	2

* Three with pyloric displacement due to posterior penetrating duodenal ulcer.

Gastroscopy is also useful in certain patients with duodenal ulcers complicated by obstruction or bleeding. Since it is sometimes difficult to determine if gastric retention is due to a duodenal or antral lesion, gastroscopic visualization of a normal pylorus would support strongly the inference that the obstruction is extragastric and probably due to a cicatrizing duodenal ulcer. In instances of shallow duodenal ulcers, bleeding intermittently and perhaps not too clearly identified radiologically, a normal gastroscopic examination would aid in ruling out gastric disease as the cause of bleeding. This may be of real significance especially if surgery is planned in a period of quiescence between hemorrhages.

GASTRIC ULCER

All patients with gastric ulcer should be examined gastroscopically if possible. The relationship of persistent gastric ulcer to cancer is fully appreciated by radiologists. It is most important not to theorize as to whether a benign ulcer will become malignant, but to admit that a gastric ulcer which fails to heal promptly should be resected.

Unfortunately, many gastric ulcers are in zones which cannot be visualized gastroscopically. Of 88 ulcers demonstrated radiographically within the previous month, 52 (59.0 per cent) were seen gastroscopically. The remainder were situated in gastroscopic blind areas or perhaps hidden by secretions or healed. Three additional ulcers were discovered, which had not been recognized radiographically. These were located high in the stomach, so that the ribs made adequate palpation during fluoroscopy impossible.

At gastroscopy the typical benign gastric ulcer has a punched-out appearance, with a gray fibrin base. If it is chronic, the walls may be thickened and elevated but nevertheless rather sharply demarcated from the surrounding normal mucosa. The wall of a carcinomatous ulcer may be expected to blend with the adjacent mu-

TABLE II: ACCURACY OF GASTROSCOPIC DIAGNOSIS OF 52 GASTRIC ULCERS

	Benign	Malignant	Equivocal
Gastroscopic opinion	35	15	2†
Opinion correct	28 (80%)*	9 (60%)*	....
Opinion incorrect	1	4	....
No follow-up or surgery refused	6	2	0

* Since the percentage of accuracy of gastroscopic diagnosis is calculated on the basis of total patients seen, it could not be decreased even if *all* cases lost to follow-up were *incorrectly* diagnosed. If accuracy of the gastroscopist's opinion is calculated solely on basis of proved cases, the results are as follows: benign ulcer, 28 of 29 correct (96.5%); malignant ulcer, 9 of 13 correct (69.2%).

† Both proved to be benign.

cosa and small nodules may be present at its edge. We are not concerned here with obviously ulcerating carcinomas, but with localized ulcerations which present no certain clinical or radiologic evidence of malignancy. The size and shape of the ulcer are of little differential significance.

If a gastric ulcer is adequately visualized, a rather accurate diagnosis of benign ulceration can be made. In at least 28 of 35 ulcers considered to be benign, the diagnosis was correct (Table II). However, if an ulcer persists after a trial of adequate therapy, the gastroscopist's opinion should not in itself bar surgical intervention. If a gastroscopic diagnosis of malignant ulcer is made, a trial of medical treatment is not indicated. When a benign ulcer is erroneously considered malignant at gastroscopy, it is usually of the callous type, which would probably be difficult or impossible to heal medically within a reasonable and safe period.

The greatest value of gastroscopy in relation to gastric ulcers is in furnishing unequivocal proof of complete healing. Since ulcers may become too shallow to retain barium, and thus can no longer be demonstrated by x-ray, gastroscopy is considered to be the sovereign method of proving that they have vanished. This presupposes, of course, that from prior examination the ulcer is known to be in an area that can be visualized with the gastroscope.

STOMAL ULCERS AND POSTOPERATIVE GASTRITIS

Depending on the meticulousness and length of follow-up, certain patients in whom stomal ulcers will develop may be identified. The incidence of gastro-jejunal ulcers is highest in those operated upon for duodenal ulcer, distinctly less in those who have had gastric ulcer, and very uncommon in those undergoing resection for gastric carcinoma. The likelihood of a stomal ulcer forming after gastro-enterostomy for duodenal ulcer may be as high as 34 per cent (6).

The most common symptoms due to pathological changes in postoperative stomachs are a feeling of fullness, diffuse upper abdominal discomfort, localized epigastric or para-umbilical pain, and unexplained melena. The functional status of the stoma may be evaluated, and a stomal ulcer may be demonstrated radiologically. If these studies are not conclusive, gastroscopy may give additional information regarding the cause of symptoms.

Gray, Meyers and Dockerty (7) have emphasized the value of gastroscopy in determining the causes of dyspepsia after gastric surgery. They found, in 25 patients who had undergone gastric surgery, 5 cases of gastrojejunal ulcer, 8 of gastrojejunitis, and 10 of gastritis.

An interesting physiologic observation is that a true sphincter action of the stoma may be seen at gastroscopy. This is apparently a function of the wall of the stomach and not caused by movements of the adjacent jejunum (8). Schindler (9) believes that a significant gastritis is far less likely to develop when this stomal sphincter action is present than when the stoma remains motionless and gaping.

In our clinic, 41 patients have undergone gastroscopy a year or longer after gastric surgery. Many of the dyspeptic complaints were functional, but nevertheless several anatomical abnormalities were found (Table III). No disease was noted at gastroscopy in 29 patients in our group. In 4 a marginal ulcer had been seen radio-

TABLE III: APPEARANCE OF GASTRIC MUCOSA IN 41 POSTOPERATIVE STOMACHS

Normal gastric mucosa	29
Superficial gastritis	7
Atrophic gastritis	2
Mucosal hemorrhages	1
Marginal ulcer	1
Jejunitis	1

graphically, but only one of these was visualized at gastroscopy. In 7 instances a bona fide gastritis was present with thick tenacious mucus adherent to the inflamed mucosa. Severe jejunitis was found in one patient with long-standing melena.

GASTRITIS

A complete discussion of gastritis and its clinical significance is not pertinent to this paper. It may be stated, however, that when clinical response to adequate therapy of peptic ulcer is poor, gastroscopy may reveal an associated gastritis as the cause of unrelieved symptoms. In a few instances, not reported here, an antral gastritis was present, associated with shallow erosions, which had been suspected radiographically. Such a type of gastritis may give pain indistinguishable from that of peptic ulcer, although more frequently the symptoms are due to a gradually developing obstruction.

SUMMARY AND CONCLUSIONS

1. Gastroscopy is of diagnostic aid in ruling out associated gastric disease when duodenal ulcers are suspected of causing chronic bleeding or obstruction, or when response to therapy is poor.

2. Benign gastric ulcers may be rather accurately differentiated by gastroscopy from malignant ulcers, but proof of benignity of an individual gastric ulcer is establishment, by gastroscopic examination, of absolute healing.

3. Significant gastritis or jejunitis may be found gastroscopically in postoperative stomachs when no roentgenologic signs of disease are evident.

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SUMARIO

La Gastroscopia en la Valuación de los Enfermos con Ulcera Péptica

La gastroscopia y la radiografía gástrica son métodos que se complementan perfectamente, capacitando la primera para observar grandes zonas de mucosa en detalle y revelando la segunda anomalías de contorno, flexibilidad o peristaltismo a la vez que mostrando lesiones en zonas inaccesibles al gastroscopio.

La gastroscopia ayuda en el diagnóstico por excluir la presencia de gastropatía asociada cuando se sospecha que úlceras duodenales ocasionan hemorragia u oclusión crónica o cuando la respuesta a la terapéutica es mala.

Con la gastroscopia pueden diferenciarse con bastante exactitud las úlceras gástricas benignas, de las malignas, pero la prueba de la benignidad de una úlcera gástrica dada consiste en el establecimiento gastroscópico de la cicatrización absoluta.

Gastroscópicamente, pueden descubrirse significativas gastritis o yeyunitis postoperatorias en estómagos sin signos roentgenológicos de enfermedad.

Peptic Ulcer

Modern Criteria for Diagnosis and Attempted Diagnosis of Healing[1]

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RADIOLOGISTS so commonly deal with objective data regarding the appearance of the stomach and duodenum fluoroscopically or on films that they are apt to lose sight of the importance of the subjective data which the clinician can bring to bear on problems related to the diagnosis of peptic ulcer or its healing. It would perhaps be of advantage to discuss with you the clinician's point of view in regard to the light thrown upon these problems by the subjective clinical data he obtains from a patient and his interpretation of the objective information furnished him by the radiologist.

The usefulness of such a discussion is apparent, for peptic ulcer is an extremely common and important disease. Sandweiss (10), in 1947, in a summary for the National Committee of the American Gastroenterological Association for the Study of Peptic Ulcer, pointed out that physicians in the United States see more than 361,000 patients a month with this condition, and estimates indicate that there are approximately one and a half million persons in this country above the age of thirty in whom peptic ulcer develops during a period of ten years. Physicians in the Armed Forces during World War II were greatly impressed by the frequency of the disease. Sandweiss quotes figures from the respective Surgeons General to the effect that during the years 1942 through 1944 for the Army and 1942 through 1945 for the Navy the number of men separated from the services for disability due to this cause exceeded 48,000, or the equivalent of at least four infantry divisions. Furthermore, its medical and financial importance as a cause of disability among veterans is indicated by studies such as those of Hussar (8). Finally, emphasis should be placed on the importance of a diagnosis of peptic ulcer among those persons in civilian life who may temporarily fail to secure life insurance or who receive disability payments on this account.

CLINICAL DIAGNOSIS

As Esterman (5) has pointed out, few lesions give rise to such typical symptoms as do uncomplicated gastric and duodenal ulcers. All of us are familiar with the pain-food-ease rhythm of uncomplicated ulcer and with the typical pain, which is chronic, periodic, usually gnawing or aching in character, and promptly relieved by ingestion of food. The two factors which strike the experienced clinician as being the most useful and certain in clinical diagnosis are (*a*) the regular occurrence of pain, distress, or related symptoms, synchronous with some phase of the digestive cycle, usually one or more hours after eating, and (*b*) the periodic occurrence of these symptoms, with alternating episodes of distress and relief for weeks or months, often without apparent cause. Of secondary diagnostic value are the location of the pain in an area between the neck and the testicle, the nature of the pain, its relief by ingestion of food or by antacids, and the associated symptoms of heartburn, belching, and gas.

How often can one obtain this "typical" history of ulcer? The more experienced the clinician, the more frequently will he, by careful questioning, elicit such a his-

[1] From the Stanford University School of Medicine and the University of California Medical School. Presented as part of a Symposium on Peptic Ulcer at the Thirty-fourth Annual Meeting of the Radiological Society of North America, San Francisco, Calif., Dec. 5–10, 1948.

tory. It is to be found in 80 to 95 per cent of all patients with active uncomplicated peptic ulcer. When there is associated gastro-intestinal bleeding, the clinical diagnosis of ulcer in the stomach or duodenum is established.

Attention should also be called to other clinical syndromes which may be encountered in patients with ulcer (Table I). Briefly, an "atypical ulcer" story is not frequent and, as Eusterman (4) has stated, in many instances its apparent occurrence is the result of incomplete or inaccurate information. The features of such an "atypical ulcer" history include frequent occurrence of pain within fifteen to thirty minutes after eating, incomplete or delayed (fifteen to thirty minutes) relief of pain by ingestion of food or antacid, absence of clear-cut episodes of distress and freedom from distress, late awakening with night pain (3 to 5 A.M.), epigastric distress on awakening, and associated general and gastro-intestinal psychoneurotic manifestations. This type of history is noted more frequently in patients with gastric than with duodenal ulceration, and it may well be the result, in part or in whole, of associated disease in other organs or of "functional disturbances" accompanying the ulcer.

Acute perforation or gastro-intestinal bleeding without antecedent symptoms of ulcer and, in the case of bleeding, without subsequent indigestion, may be the only clinical manifestation of an active peptic ulcer. Or the sole clinical evidence may consist in symptoms of other complications, such as penetration or obstruction of the pylorus, particularly in patients of the hyposensitive type. Finally, and infrequently, the only clinical manifestation may be pain of a crisis type or vomiting, much like that observed in the crises of tabes dorsalis.

Chronic dyspeptic symptoms, such as gaseous indigestion, cramping abdominal pains, abdominal distention, belching, and aerophagia are comparatively rare in cases of simple ulcer, as has been pointed out by Bockus (2). On the other hand, a "typical ulcer story" may occasionally be obtained from patients with carcinoma of the stomach, cholecystic disease, chronic pancreatitis, carcinoma of the pancreas, or hookworm infection. Usually the skilled clinician can find in the patient's history evidence to lead him to suspect a lesion other than ulcer. The so-called "pseudo-ulcer" or "atypical ulcer" story is much more commonly given by patients with psychoneuroses than by patients with ulcer.

TABLE I: CLINICAL FEATURES OF ULCERS

Manifestations	Features
Typical history	Pain
	(*a*) Synchronous with digestive cycle
	(*b*) Occurring periodically
	(*c*) Chronic
	(*d*) Special qualities
Atypical history	Lack of clear-cut ulcer features (see text)
Symptoms of complications	Often absent or minimal antecedent dyspepsia
(*a*) Hemorrhage	
(*b*) Perforation	
(*c*) Obstruction	
Crisis type	Vomiting
	Pain

Other clinical data, including those obtained on physical examination, gastric analysis, or other laboratory tests, generally are not of much value in the diagnosis of uncomplicated peptic ulcer, although they may be of help in the occasional case.

The clinical diagnosis depends, in brief, on the history the patient gives, and in cases difficult to diagnose, considerable skill may be required of the clinician to approach the patient properly and to elicit a true account of his symptoms.

RADIOLOGIC DIAGNOSIS

It is generally accepted that the radiologic method of diagnosis of peptic ulcer is 95 per cent accurate. A crater or niche is the only definite x-ray evidence of an active ulcer. It is reported to be found in approximately 90 per cent of patients with gastric ulcer and in from 30 to 70 per cent of cases of duodenal ulcer. The variability in results depends in large part on the technic of examination. In a considerable

number of cases of active ulcer a crater will not be demonstrable and furthermore a niche has at times been reported in the stomach or duodenum when examination within the next few days, at gastroscopy, at operation, or at necropsy, has failed to reveal an active ulcer.

Constant duodenal deformity in the absence of a previous upper abdominal operation generally is considered to be evidence of an active or healed duodenal ulcer and as such is said to be from 90 to 95 per cent accurate. Other less convincing and suggestive evidence of duodenal ulcer includes irritability, spasm and fragmentation of the duodenal cap, and edema of or striking alteration in the appearance of the duodenal or gastric mucosa. Most of the errors that are made in the radiologic diagnosis of peptic ulcer are those of omission and not of commission.

CORRELATION OF CLINICAL AND RADIOLOGIC DIAGNOSIS

In making a diagnosis of peptic ulcer, the roentgenologic evidence must be weighed and its value assessed by the clinician in conjunction with the other data available. As Eusterman (5) has well expressed it, "the case history, in the absence of skilled fluoroscopy, is all-essential, and is much more important than unskilled examination by fluoroscopy alone."

Perhaps most often for his own reassurance and that of the patient, the clinician will request radiolgic examination to rule out an intrinsic organic lesion in the upper gastro-intestinal tract in the presence of digestive symptoms of uncertain nature. In performing this function the clinician leans heavily upon the well trained radiologist.

In determining the activity of a duodenal ulcer, the experienced clinician will much more often rely on absence of symptoms than he will on the radiologist's report. If the patient is symptom-free, disappearance of a previously known crater substantiates the evidence of healing. However, if duodenal deformity persists, the clinician knows that the radiological examination is not helpful in telling him whether an ulcer is active or inactive.

Garland (7) has presented a very good outline of the report which the radiologist might give the clinician on patients referred for roentgen examination for evidence of duodenal ulcer, namely: (1) duodenal ulcer with visible crater; (2) duodenal ulcer with questionable crater; (3) duodenal ulcer with no crater visible but deformity, typical, presumably active; (4) duodenal bulb deformity, probably scarring from healed ulcer; (5) duodenal bulb deformity probably surgical (closure), perforated ulcer, etc; (6) duodenal bulb deformity, probably extrinsic (no ulcer); (7) negative.

It is suggested that this classification might be modified so that Item 5 would read "duodenal bulb deformity with pyloric obstruction and/or gastric retention," omitting any reference to the therapeutic indications.

While a classification of this type is very useful for purposes of study, it must be recalled that, without anatomic proof of the exact appearance of the duodenal mucosa, these findings must in large part be interpreted by the clinician in terms of the patient's symptoms and the clinical findings, and that they are therefore of relative and not absolute value. Use of such a classification by a radiologist in conjunction with several carefully trained clinicians would, over a period of five or ten years, add considerably to the diagnostic accuracy of each group, and above all would lead to more information for each of them.

When the radiologist reports findings in agreement with the clinician's impressions of the diagnosis, the diagnosis is established. When there is a discrepancy, however, between the clinical and radiological findings, the clinician will be influenced in his diagnosis by such factors as (1) the character of the patient's complaints and their resemblance to the symptoms of ulcer, (2) the certainty of his clinical impressions of ulcer, (3) his past experience

TABLE II: CORRELATION OF CLINICAL AND RADIOLOGICAL DATA IN DIAGNOSIS OF ULCER

Method of Diagnosis	Value of Signs				
	Absolute	Definite	Relative	Questionable	
Clinical	95 per cent Pain synchronous Periodicity	85–90 per cent Ulcer type of distress	75–85 per cent Dyspepsia suggestive of ulcer	50–60 per cent No distress or vague distress	Ulcer type distress
Radiologic	Niche	Persistent duodenal deformity	Fragmentation of cap Various defects, spasm, irritability, etc.	Duodenal deformity	Normal duodenum

with the accuracy of reports from the radiologist who examined the patient, and (4) the presence of other evidences of organic disease.

In Table II an attempt has been made to set down those clinical and radiologic data which would be considered to have absolute, definite, relative, and questionable value in the diagnosis of ulcer.

In a patient with clinical evidence or a "typical history" of ulcer, with or without bleeding, and a radiologically demonstrable niche in the stomach or duodenum, the diagnosis of ulcer would be established (with the exception of ulcerating neoplasm in the stomach). In fact, with either of these clinical or radiologic findings alone, the diagnosis of ulcer could be made and be accepted unless some very unusual mitigating circumstances pointed strongly to another condition. Furthermore (in a patient with ulcer type of distress) with a constantly deformed duodenal cap the diagnosis of duodenal ulcer would be established. These findings would have definite value (Table II). In a case, however, in which the dyspepsia was suggestive of ulcer and the radiologic examination indicated variable deformity, spasm, irritability, or fragmentation of the duodenal cap, these latter findings would be relative only and the physician (to come to a correct decision) would have to be guided by his clinical judgment, by the subsequent clinical course, and subsequent radiological appearance of the duodenal bulb.

In a rather large and important group of cases there is conflict between the clinical and radiologic data. For example, the patient may have no history, or a very vague one, of dyspepsia, and yet show a constant duodenal deformity; or, conversely, the patient may give a classical story of ulcer while the stomach and duodenum appear normal radiologically. In this group of puzzling cases, all sorts of variations may be noted, in the clinical range of "no symptoms" to "those of ulcer" and in the radiologic range from "a normal stomach and duodenum" to a "constant deformity or niche."

Too often, in his effort to cover himself, the radiologist will report changes in the mucosa of the stomach or duodenum which could or could not be interpreted to mean ulcer. These changes include edema of the mucosal folds, irregularity of the folds, or a "drop" of barium pent up between them. While such findings should be accurately recorded, too often they are interpreted by the radiologist as perhaps those of ulcer or they are looked upon by the clinician and even by the patient as significant of disease. When radiologic findings of an indefinite nature are made, the clinical findings and the results of subsequent radiologic examinations should be given most weight.

How is such a situation to be resolved for the clinician and his patient? The only courses open are: (1) further roentgenologic study by the same or another radiologist; (2) observation of the patient under treatment, with subsequent radiologic examination; (3) gastroscopy in case of a suspected lesion in the stomach; (4) operation.

Further Radiologic Study: At times it is unfortunate that in cases of peptic ulcer the clinical data are based largely on the

history and are therefore subjective while the radiological data are chiefly objective. When there is disagreement between the two physicians, patients, relatives, insurance companies, government agencies, and the courts are apt to overemphasize the importance of x-ray films—and particularly a typewritten report signed by a radiologist—in contrast to the subjective data of the clinician, which lacks "proof."

As a clinician, it occurs to me that when the patient has a story which suggests ulcer and the radiologist reports normal findings, the logical thing to do is to repeat the radiological examination immediately and/or after an interval of several weeks. Too often radiologists are sensitive about being asked to repeat examinations. Such a radiologist has not learned to accept what clinicians long since have accepted as essential to establishing a diagnosis in a difficult case—namely, repeated examinations, as of the heart, of a questionable abdominal mass, or an unusual cutaneous lesion. Furthermore, it would be most helpful if such immediate "repeat examinations" were considered part of a radiologic consultation and not charged for at full rates. Finally, we should not so frequently neglect, in a difficult case, to ask another radiologist to examine the patient in consultation. Such practice would not only lead to better diagnosis but it would help further to develop the attitude that a radiologist is a physician, consulting on a patient and expressing an opinion, not merely a technician whose report is to be accepted blindly like the laboratory report of a urinalysis or blood count.

Observation of the Patient Under Treatment, with Subsequent Radiologic Examination: If further radiologic study and consultation do not confirm the clinical suspicion of peptic ulcer and the patient's history is very suggestive of that diagnosis, the sensible course is to observe the results of a therapeutic trial and subsequent radiologic examination. Careful consideration should be given not only to relief of ulcer symptoms but also to the persistence or development of others, such as anorexia, abdominal pain, diarrhea, and loss of strength or weight, to changes on physical examination, including abdominal tenderness and masses, and to laboratory data which indicate anemia, achlorhydria, and gastric retention. If symptoms persist or if new symptoms or changes in physical findings occur, further roentgenologic study of the stomach and duodenum is indicated in from four to six weeks. Further radiologic examination is also indicated if symptoms recur following discontinuance of a therapeutic program.

Gastroscopy: Gastroscopy may be helpful in establishing a diagnosis of ulcer in the stomach in certain cases in which there are symptoms suggesting ulcer, in patients with asymptomless bleeding, and in suspected lesions in the stomach or lesions the nature of which is uncertain on radiological examination.

Operation: In the event that repeated radiologic examination proves negative in a patient with a clinical history strongly suggestive of ulcer, indications for operation are similar to those in cases in which an ulcer is known to be present. That is, if pain is intractable, bleeding continues, or evidence of obstruction persists, there should be no hesitation in advising operation even though the radiological examination gives negative results.

Cases in Which the Radiological Examination Indicates Ulcer But the Clinical Data Are Negative: Not uncommonly radiologists report the presence of gastric or duodenal deformity, spasm, irritability, or even a niche in a patient without apparent clinical evidence of ulcer. These findings are perhaps most frequent when vague abdominal pain or symptoms are present, or when the radiological examination is done for purposes of reassuring the patient, and occasionally the physician, that everything is all right.

How much attention is to be paid to such a report? A great deal depends on the nature of the finding, which, in such circumstances, should always be confirmed by repeated examinations. If a definite crater is visible, the likelihood of an active

ulcer is strong. Much less significance, naturally, would be attached to such findings as constant deformity of the duodenal bulb, or irritability, spasm, edema, or alteration in the mucosal folds. These may simply represent scarring from a previous ulcer. In his evaluation, the clinician would be influenced considerably by such factors as his previous experience with the radiologist reporting the finding, the presence of symptoms and their nature, the location of the "lesion" in the stomach or duodenum, accessory findings, such as those of gastric analysis, and evidence of disease in other organs.

Certainly most careful study should be made of apparent abnormalities in the stomach, and full attention be paid to gastroscopy, gastric analysis, and other methods of examination. The wisest course would seem to be to ignore minimal findings in the duodenum unaccompanied by clinical symptoms and to attempt a therapeutic trial, followed by re-examination in four to six weeks, in patients with more striking change in the absence of symptoms. In the absence of an apparent gastric lesion or a niche in the duodenum, the clinician should not be too readily swayed by radiologic findings if symptoms be absent.

EVIDENCE OF HEALING OF AN ULCER

(*Table III*)

Clinical Evidence: Can it be reliably determined clinically that an ulcer is healed or active? The strong tendency of ulcers to heal and to recur complicate this whole problem and have led some clinicians to the view that the ulcer itself—at least in the case of duodenal ulcer—may not be of great importance except as it produces complications. According to Bloomfield (1) it is of less than prime clinical importance to decide whether a deformed bulb means active or healed ulcer, since such a "healed" lesion is very likely to show activity time and again in the future. From the standpoint of "disposition" of a case in military service, or of determining compensation in the case of a veteran or other civilian, it may, however, be important to decide whether at a particular time an ulcer is healed or active.

TABLE III: CRITERIA OF HEALING OF PEPTIC ULCER

Type of Examination	For Healing	For Activity
Clinical	None Absence of symptoms for 6–12 months?	Persistence of symptoms or bleeding
Radiologic	1. Disappearance of niche 2. Diminution or clearance of spasm, retention, deformity, irritability (suggestive only)	Persistence of niche
Gastroscopic	Disappearance of crater	Persistence of crater

Clinical evidence for healing is almost completely lacking. It goes without saying that an active ulcer may not produce symptoms, particularly if the patient has been placed on medical treatment. Consequently, lack of symptoms is not a criterion for healing. Perhaps the only reasonable statement which can be made is that if a patient with known previous ulcer has gone for a period of one year without treatment and without symptoms of ulcer or bleeding, healing has occurred. On clinical grounds alone, this statement cannot be proved and, for ordinary purposes, it is useless without radiologic evidence to substantiate it.

The disappearance of occult blood from the stool or its absence is not satisfactory evidence of healing or of healed ulcer. In the case of gastric ulcer, gastroscopic examination may be helpful in determining whether healing has occurred if the lesion is in an area which can be directly observed. Actually the clinician can more accurately determine activity of an ulcer than he can its healing, for continuance of symptoms, particularly if bleeding is present, indicates activity.

Radiologic Evidence: How accurately can the radiologist determine the healing of an ulcer and what criteria can be used to determine healing?

In the case of gastric ulcer, the radiologist can usually determine healing very accurately by observing disappearance of the niche. Only occasionally will the gastroscopist find an active gastric ulcer when the radiologist reports it to be healed, although not infrequently the gastroscopist will find an ulcer incompletely healed when the niche is no longer visible on radiologic examination.

For duodenal ulcer the radiologic evidence of healing is less convincing. Disappearance of a niche in the duodenal bulb may be considered as evidence of healing, and it has been so used in studies such as those of Cummins, Grossman and Ivy (3) on the "healing" time of ulcer. If, in addition to disappearance of the niche, there is disappearance of the duodenal deformity, the radiologic criteria for healing are complete and convincing (Garland, 7). However, Feldman (6) has correctly pointed out that disappearance of the niche cannot always be relied on as a sign of complete healing. Other observers, such as Jordan (9), consider fluoroscopy the best aid in distinguishing active from quiescent ulcer, since rapid filling and emptying and spasm (of the bulb) are so characteristic of the active phase.

During the war, extensive and frequent radiologic examinations of young men with duodenal ulcers of short duration indicated very definitely that complete restitution of the duodenal cap to normal may occur following treatment. This observation is in conflict with the often expressed view that once a duodenal ulcer has been present the bulb never again becomes smooth or normal in contour.

Weir (11) well expressed the average clinician's view of the radiologist's capacity to determine healing of duodenal ulcer when he stated: "However, because roentgenologic diagnosis of duodenal ulcer depends on the persistent deformity of the cap, craters are demonstrable in only 20 to 40 per cent of cases, and because this deformity usually persists after healing, there remains no satisfactory roentgenologic finding by which the activity, inactivity, or healing state of duodenal ulcer can be determined." Similarly Garland (7) has indicated, in summary, that in average circumstances the reliability of x-ray examination in determining healing of duodenal ulcer is probably only 50 per cent.

Consequently, it seems reasonable to conclude that when, in a case of duodenal ulcer, a once visible crater disappears following therapy and the patient becomes free of symptoms, healing has occurred. If, in addition, the duodenum has again become normal, the evidence is even better. Many clinicians in such cases would be skeptical of the original roentgen findings and diagnosis. In the absence of a crater, the radiologist can produce almost no evidence of the healed or active state of an ulcer in the duodenum.

Information Which the Clinician Expects from the Radiologist: In the diagnosis of peptic ulcer, the clinician always feels most satisfied when the clinical and radiologic data are in agreement. Therefore, in the patient suspected of having an ulcer, the clinician expects information (1) as to the presence or absence of ulcer; (2) as to whether or not the ulcer is healed or active; (3) as to the location of the ulcer—gastric, duodenal, or jejunal; (4) as to the presence or absence of obstruction, and, if gastric retention is present, whether it is due to actual obstruction, spasm, edema or scar tissue or to gastric atony; (5) as to the size of the ulcer; (6) as to its shallow or penetrating character; (7) in the case of a gastric lesion whether or not it is malignant.

CLINICAL INTERPRETATION OF RADIOLOGIC STUDIES OF THE UPPER GASTRO-INTESTINAL TRACT

How much attention does the clinician practising internal medicine pay to radiologic studies of the upper gastro-intestinal tract and why does he have such studies made?

In an effort to come to some opinion regarding this matter, a review has been made of 200 consecutive cases in which such studies were done by radiologists for

a group of physicians practising together in the same office. No conclusions can be drawn from such a study, as the series is small, and in only a few cases was either the clinical or the radiological diagnosis actually confirmed by anatomic or pathologic study of the stomach and duodenum. The results, recorded in Tables IV and V, are striking and require some explanation.

TABLE IV: UPPER GASTRO-INTESTINAL RADIOLOGIC STUDIES IN 200 CONSECUTIVE CASES: ANALYSIS OF CLINICAL INDICATIONS FOR RADIOLOGIC STUDY

	Cases
"Ulcer story"	41
Dyspepsia	54
Vague abdominal symptoms	70
Reassurance to patient	6
Other	29
TOTAL	200

In 4 cases the radiologic diagnosis of gastric ulcer was not concurred in by the clinician in his final diagnosis because the clinical evidence of ulcer was insufficient and he did not consider the radiologic findings convincing. The final outcome in these 4 cases is not known. In 4 cases the radiologist's diagnosis of gastric ulcer was accepted. In 11 cases in which the radiologist reported finding a duodenal ulcer the clinician did not accept the diagnosis because of insufficient clinical evidence in 8, lack of free hydrochloric acid in the gastric juice (after stimulation with histamine) in 1, and for unknown reasons in 2 cases.

In 3 cases in which a final diagnosis of carcinoma of the stomach was made the radiologic diagnosis of carcinoma was definite in one case only. In a second case the radiologic diagnosis was "probably scarring on lesser curvature (healed ulcer?)," the preoperative clinical diagnosis was questionable neoplasm of the stomach, and operation revealed an inoperable carcinoma of linitis plastica type. In a third case, that of a woman of thirty-eight with a brief history typical of ulcer, the original radiologic study revealed irregularity and swelling of the mucosal folds in the duodenal bulb, without evidence of an ulcer crater. Fifteen months later two radiological studies within a ten-day period revealed gastric retention and pyloric obstruction apparently due to spasm. A month later pyloric obstruction persisted and the radiologist reported "may be ulcer, neoplasm to be strongly considered." Free hydrochloric acid of well over 100 clinical units was present, a clinical diagnosis of duodenal ulcer with obstruction was made, and at operation an ulcer crater in the stomach was found, at the base of which evidence of carcinoma was disclosed by microscopic study (lymph nodes were involved also).

It is interesting to note what interpretation the clinician placed on the radiologist's report of "irritability" or inflammatory changes in the stomach or duodenum (usually the latter) (Table IV, 32 cases). A final clinical diagnosis of gastric and duodenal ulcer was not made in any of these cases; carcinoma of the stomach was diagnosed in 2 cases, "functional" gastro-intestinal diseases in 14 cases, anxiety tension states in 9 cases, and other non-gastro-intestinal disease in 7 cases. It is worthy of comment that in about half the cases referred for radiologic study the roentgenologist reported normal findings.

TABLE V: UPPER GASTRO-INTESTINAL RADIOLOGICAL STUDIES IN 200 CONSECUTIVE CLINICAL CASES

Radiological Diagnosis	Cases	Final Clinical Diagnosis	Cases
Gastric ulcer	8	Gastric ulcer	4
Duodenal ulcer	43	Duodenal ulcer	32
Tumor of stomach	1	Carcinoma of stomach	3
"Irritability" or inflammatory changes	32	"Functional" gastro-intestinal tract disease	46
Other (including varices, hernia, duodenal polyp, subtotal gastric resection, etc.)	15	Anxiety—Nervous exhaustion	51
Normal	101	Other gastro-intestinal tract diagnoses	64
TOTAL	200	TOTAL	200

TABLE VI: RADIOLOGIC DIAGNOSES IN 200 CASES CLASSIFIED ACCORDING TO CLINICAL INDICATIONS FOR RADIOLOGIC STUDY

Clinical Indications	No. of Cases	Radiologic Diagnoses					
		Gastric Ulcer	Duodenal Ulcer	Carcinoma Stomach	Irritability or Inflammatory	Other	Normal
Ulcer story	41	4	24	1	7	2	3
"Dyspepsia"	54	2	7	0	9	6	30
Vague gastro-intestinal symptoms	70	2	8	0	10	2	48
Reassurance	6	0	1	0	0	0	5
Other	29	0	3	0	0	5	16

It is of some interest to note the clinical indications which led the internist to request radiologic study in these 200 cases (Table V). Under "dyspepsia" are included patients complaining of "gas," upper abdominal discomfort or distress, belching, heartburn, nausea or vomiting related to eating but without the features of an "ulcer story" previously noted. "Vague abdominal symptoms" include abdominal complaints not clearly related to ingestion of food; this group, however, cannot be sharply separated from the group with dyspepsia. The term "other" covers patients with complaints or previous findings of "gas," diarrhea, constipation, anemia, hiatal hernia, black stools, achlorhydria, motion sickness, migraine, and so forth. The results of radiological studies in these various groups of patients are noted in Table VI.

The observations which can be made from this small series of cases are that the radiologist made the diagnosis of gastric and duodenal ulcer more frequently than the clinician was willing to accept it; that when the radiologist reported irritability or inflammatory change in the stomach or duodenum, a diagnosis of ulcer was not made clinically in a single instance, and that when a clinical history typical of ulcer was present the radiologist made a diagnosis of gastric or duodenal ulcer in 28 of 41 cases and reported findings of a normal stomach and duodenum in only 3. While these observations are interesting, no final conclusions can be drawn from them in view of the selective character of the cases and, as pointed out above, the lack of anatomic diagnoses.

Certainly closer co-operation is needed between radiologist and clinician in the study of patients in whom there is a discrepancy in findings, and further studies should be carried out.

SUMMARY

The clinical diagnosis of peptic ulcer depends upon the history given by the patient. The so-called "typical history" is present and is diagnostically accurate in 80 to 95 per cent of all cases. In others there may be an "atypical" story, the symptoms may be due to complications, or there may be pain or vomiting of the crisis type.

Radiologic diagnosis, which is said to be 95 per cent accurate, depends largely on demonstration of a gastric or duodenal niche or constant deformity of the duodenum.

When there is a discrepancy between the clinical and radiologic findings the clinician will be influenced in his diagnosis by such factors as: (1) the character of the patient's complaints and their resemblance to the symptoms of ulcer; (2) the certainty of his clinical impression of ulcer; (3) his past experience as to the accuracy of reports from the radiologist who examined the patient; (4) the presence of other evidence of organic disease; (5) the results of subsequent clinical and radiologic observations of the patient.

There is no satisfactory clinical evidence of healing of an ulcer. Persistence of symptoms probably means activity of the lesion, but the reverse does not hold. Radiologic evidence for healing is unsatisfactory, also, although disappearance of the niche and the occasional return of the

duodenal bulb to normal probably indicate healing.

Interesting but inconclusive observations were made in correlating the findings in 200 consecutive cases in which clinical and radiologic studies of the upper gastrointestinal tract were done.

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SUMARIO

Ulcera Péptica: Modernas Pautas para su Diagnóstico y para Tratar de Diagnosticar su Curación

El diagnóstico clínico de la úlcera péptica se basa en los antecedentes comunicados por el enfermo, pues hay presente la llamada "típica historia," que resulta diagnósticamente exacta en 80 a 95 por ciento de todos los casos. In otros, la historia puede ser "atípica," los síntomas pueden deberse a complicaciones, o puede haber dolor o vómitos del tipo crítico.

El diagnóstico radiológico, que pasa por alcanzar una exactitud de 95 por ciento, se basa en gran parte en el hallazgo de un nicho gástrico o duodenal o de deformidad constante del duodeno.

Si discrepan los hallazgos clínicos y radiológicos, el clínico considerará en su diagnóstico factores tales como: (*1*) naturaleza de los síntomas y semejanza a los producidos por úlcera; (*2*) certeza de su impresión clínica de úlcera; (*3*) exactitud de los informes suministrados en el pasado por el radiólogo que examinó al paciente; (*4*) presencia de otros signos de afección orgánica; (*5*) resultados de las subsiguientes observaciones clínicas y radiológicas del enfermo.

No hay signos clínicos satisfactorios de la cicatrización de una úlcera. La persistencia de los síntomas denota probablemente actividad de la lesión, pero lo contrario no es siempre cierto. Los datos radiológicos de cicatrización tampoco son satisfactorios, aunque probablemente la indican la desaparición del nicho y el retorno ocasional del bulbo duodenal a lo normal.

Fueron interesantes, pero no terminantes, las observaciones realizadas al correlacionar los hallazgos en 200 casos consecutivos en los que se ejecutaron estudios clínicos y radiológicos de la porción superior del tracto gastrointestinal.

(*For discussion of papers in preceding symposium on Peptic Ulcer, see following page*)

DISCUSSION

(Papers by Templeton; Harris; Morgan; Dailey; Wilbur and Watts)

Merrill C. Sosman, M.D. (Boston, Mass.): It has been a pleasure to be here and listen to this Symposium. There does seem to be a little controversy—Templeton *vs.* Harris—but I believe that can be resolved historically. In my thirty years of experience, I think that the stages of gastro-intestinal examination can be laid out pretty definitely. Originally, it was mostly by films alone, as exemplified particularly by Lewis Gregory Cole of New York. The second stage was fluoroscopy, represented by Russell Carman and popularized by him, employed at times, unfortunately, in some clinics, without any films at all. The third stage (which most of us are in at the moment) is the use of fluoroscopy to locate the condition and spot films to identify it, and I think that Dr. Templeton was advocating that we go into the fourth stage—that of making routine spot films in all parts of the gastro-intestinal tract under examination, in addition to the regular films and the complete fluoroscopic study. If that is true, Dr. Templeton, I would like you to tell us exactly what you want us to do in the way of more numerous spot films and examinations. Are you going to take these for every patient, or only for those who have a positive history or some evidence of definite disease? Are you going to take them in a partly filled stomach? In an upright, prone, supine, or lateral position? It would make a tremendous amount of work out of one single examination if you wanted to do it thoroughly. I would like a detailed plan of what you recommend.

I think that most of us modify our examinations, depending either on the patient's symptoms, on the history (which is either sent to us with the patient or which we must take ourselves), or, finally, on what we see during fluoroscopy. We cannot repeat exactly the same examination in each individual case. We have to modify it depending on what we hear, or what we suspect, or what we see.

Now, for the second paper—Harris *vs.* Templeton. I think that Dr. Harris has an excellent technic in fluoroscopy, but it is absolutely impossible to tell how many cases he has missed. He does not have the spot films to show us and prove to us that lesions were absent in those individual cases. Unless every one of those cases was also examined by Dr. Templeton, using the spot-film technic, and all of Dr. Templeton's cases were re-examined by Dr. Harris without spot films, I don't know where we stand. I would like to have those two get up and fight it out together.

The determination of activity in duodenal ulcer by the spot-film technic is impossible, I think, in 15 to 20 per cent of the individuals; either the duodenal cap is too high above the rib margin, or it is difficult to get satisfactory compression, or the abdominal wall is too thick and muscular for adequate study. Therefore, there would be a group of patients—15 to 20 per cent—in whom a duodenal ulcer could not be ruled out, because, in certain individuals, there is an active duodenal ulcer with no deformity of the bulb. In my experience, that occurs almost entirely in young people with a short history of gastro-intestinal disability, and this history is often typical, as Dr. Wilbur has said. When those ulcers heal, they are apt to heal entirely. They have no deformity to start with, so the ulcer will disappear and the cap will be perfectly normal unless there is a recurrent ulcer.

Another point, Dr. Harris, is your mention of antispasmodics. That seems to be in all the books. I am afraid that it is even in Dr. Templeton's book. From my own experience, I think that the use of antispasmodics is a lot of hooey. I don't believe that they do a single bit of good. I have not seen any evidence of a patient being helped by them. I get much more benefit from simple re-examination of the patient fifteen minutes after he has relaxed in the waiting room while I am examining another patient. I think that is much more beneficial than a barrel full of antispasmodics.

Dr. Morgan has presented a beautiful paper, but one certainly needs to read it in detail and study it carefully in order to appreciate it thoroughly. Here are facts—not just opinions. I certainly would agree that an automatic timer which records the duration of fluoroscopy should be an essential part of every fluoroscope and that the time of fluoroscopy should be recorded on the patient's chart. We all agree that a small aperture—just enough to see the part that we are looking at—is important. The new bright fluoroscopic screen allows us to cut down the milliamperage, which in turn reduces the radiation hazard to the patient and also to the observer. I am going right back home and put lead-rubber aprons on the edge of the screen, such as those used with the new, heavy, cumbersome fluoroscopes to which Dr. Harris objected. I am referring to the little flexible rubber apron which will cover up the area between the screen and the top of the table. This can be put at the end of the screen when we are doing horizontal fluoroscopy and can be swung to the bottom when we are doing upright fluoroscopy to cover that area between the screen itself and either the top of the apron or the top of the lead-backed chair. The amount of scattered radiation around the edge of the fluoroscope is rather alarming.

Dr. Morgan's facts as to visibility should re-

solve the argument between Dr. Harris and Dr. Templeton, as they are certainly in favor of multiple films taken in different positions and with different degrees of filling. I am very glad to see that the hazard from spot films is much exaggerated. I know you all noticed the statement that one could take six spot films with only about a fifth of the exposure involved in five minutes of fluoroscopy. I have repeatedly told my residents that they cannot make a good diagnosis without good films. That is one of the first essentials, and good spot films certainly are essential in gastro-intestinal diagnosis.

We agree entirely with Dr. Dailey that gastroscopy supplements x-ray examination and is not in competition with it. I am very glad to hear you express that point of view, Dr. Dailey. The gastroscopist can show superficial erosions and definite gastritis which we cannot diagnose either by fluoroscopy or by any number of films. It is also quite valuable in demonstrating the healing of an ulcer as well as in forming an opinion (not necessarily a fact) as to whether an ulcer is malignant or benign when we are in doubt following an x-ray examination.

In my experience, practically every duodenal ulcer which is chronic is associated with thick, tortuous, gastric mucosal folds. I have been in the habit of calling these "gastritis," but since we have had a good gastroscopist, I have realized my mistake. I am sure that, as Dr. Dailey has pointed out, they are purely edema of the mucosa. Therefore, we now limit the diagnosis of "gastritis" to those patients who not only have long, thick, tortuous rugae, but also evidence of hypersecretion, and I think that the combination of big rugae and fluid comes out almost 90 or 95 per cent in accord with the gastroscopic findings. Usually patients with gastric hyperacidity show the same thick edematous mucosa, but in only a few cases is there enough actual inflammation to be called gastritis. On the whole, the size of the gastric rugae, to me, has been a pretty good index of the degree of hyperacidity; the higher the acidity, the greater the edema of the gastric mucosa. I would like to have Dr. Dailey and Dr. Wilbur comment on that if they will.

Dr. Wilbur, unfortunately, did not have sufficient time to read his entire paper. However, the paper will be published, and I recommend that you read it in detail. It gives the clinician's idea as to what the radiologist should furnish him. My own experience in one year of consecutive gastro-intestinal examinations covering about 1,500 cases showed that exactly one out of four patients had duodenal ulcers; 50 per cent of the patients with sufficient symptoms to justify an x-ray examination were entirely negative. Autopsy findings, with careful study of the duodenal bulb, have shown that 10 per cent of all people have duodenal ulcer. Therefore, in this audience of approximately 500, there are 50 who either have had, have, or will have ulcer during their lifetime. One can sometimes tell by the discussion from the stage who has the ulcers.

There is one thing that I would like to add to your paper, Dr. Wilbur, which may explain some of the discrepancy between the clinical symptoms and history and the x-ray findings. The fact is that the clinician is very prone to try an anti-ulcer diet on the patient for two or three weeks before referring him for x-ray examination, and in many such cases, I am sure that an ulcer will heal entirely in that time. This may be the cause of the discrepancy. I think that this practice is to be condemned, and I recommend that the radiologist ask the patient whether or not he has been on an ulcer diet before the x-ray examination.

The question of repeated examinations is also quite important, and I feel that we should reduce the cost of a gastro-intestinal study as much as possible to make these more feasible. However, that is another problem and should not be brought up here.

A third thing is this: Rumor has it that if a patient has chronic duodenal ulcer, he is exempt from the possibility of gastric carcinoma. I would like to put in one strong vote against that opinion, as I have often seen gastric carcinoma in a patient with the scar of an old duodenal ulcer.

Another possible explanation for some of the discrepancy referred to by Dr. Wilbur, I believe, is the fact that older patients may have the scar of a previous ulcer which gave them plenty of symptoms when they were young, but, as the gastric acidity dropped with age, those symptoms disappeared. Yet one can still find the scar of the old ulcer. The patient, however, may have no ulcer symptoms at the time.

Joseph C. Bell, M.D. (Chairman): Dr. Templeton, will you come forward and defend yourself?

Dr. Templeton: Thank you, Dr. Sosman, for your discussion. Your speaking of the fourth phase brought to mind the fourth dimension. It is pretty hard to define and clarify.

I didn't have time to go into the technic of the gastro-intestinal examination. I shall leave that for my Refresher Course.

There are some key films that one can take when no abnormality is recognized at fluoroscopy. As a rule, these key films help in difficult situations. Take one view as the barium enters the stomach. Take one view of the gastric body after the patient has taken two ounces of barium, and while exerting light pressure. The amount of pressure depends on the thickness of the abdomen. There should be just enough to bring out the folds. Do the same thing with the antrum. In the average stomach, two or three spot views suffice to cover these parts if one uses quarters of 8 × 10's. In the larger stomach, three or four views

are needed. After this, take radiographs of the filled-out and compressed duodenal bulb.

Dr. Sosman raised a question regarding the short, heavy-set patient, in whom the lesion cannot be seen by fluoroscopy because the stomach is located beneath the ribs and cannot be compressed. When the abdomen is large, we turn the patient onto his abdomen, and then onto his back cocked toward the left side. The bulb is high. Air will run into it. In a large percentage of the cases one obtains a double contrast view of the bulb. In this way I have seen a number of ulcers which would not have been detected with the patient standing.

With the patient supine, films of the cardiac end filled with barium are made. With the patient turned toward his left side, the beam cuts on across the posterior wall and shows this segment. In all, eight exposures are made on two 8 × 10 films. This is the average number of exposures.

Now, about antispasmodics. I am reminded of the radio quiz-master who quoted one of the participants, only to find that this man didn't recognize what he had written. I think, however, that I did not advocate antispasmodics. I believe that any favorable effect obtained by their use is more or less psychologic in origin. When the patient returns the second time he is more at ease, as he knows what is going to be done. I think that this changed mental attitude plays a major role in the success of the examination.

Now I am going to ask questions about the small focal spot *vs.* the large spot. From a theoretical standpoint, Dr. Morgan has shown that one can see more with the small than with the large spot. Of how much significance is this? Does it really help with fluoroscopy? Is the difference great enough to be of practical significance?

Leo G. Rigler, M.D. (Minneapolis, Minn.): There is so much meat for discussion that it is quite difficult to restrain oneself. I might say that the fourth stage in gastro-intestinal examination, of which Dr. Sosman spoke, was reached in Sweden about twenty years ago, where the fluoroscope was used for purposes of localization both as to the chest and the gastro-intestinal tract. One difficulty, however, is that you become so intent upon getting the patient in the proper position for the films that you are likely to lose sight of the primary examination, *i.e.*, the fluoroscopic examination.

We have had rather a long experience in this respect, not with peptic ulcers, but with tumors, in which we have used fluoroscopy alone, fluoroscopy with spot films, and with conventional radiographs made in a variety of positions, and my own feeling at the present time is that I wouldn't want to do without any of the three if I were trying to find small lesions, polyps, for example, 3 or 4 mm. in diameter. We thought that we saw them under the fluoroscope, but we were not at all certain of it. However, we were able to confirm them by spot films.

We know that we have missed carcinomas of 1 cm. diameter in the most painstaking fluoroscopic examinations, and we know that we have seen small tumors, measuring say 2 or 2.5 cm. in diameter, by fluoroscopy, have demonstrated them by spot films, and then managed to eliminate them completely in conventional radiographs taken with both filled and empty stomach. A great part of the data on this question is based on the introduction of foreign bodies, but that is scarcely comparable.

I feel very strongly at the present time that, at least for small tumors, we need all three media to arrive at a proper diagnosis.

I was somewhat amazed at Dr. Wilbur's figures as to the discrepancy between the presence of ulcer, radiographically, and the history, because I don't know of any good data which will support the thesis that a good history means that an ulcer is present. As a matter of fact, I think that most autopsy studies indicate that the history is a very vulnerable criterion for the presence or the absence of ulcer. I would certainly be reluctant to accept the idea that the history, regardless of how carefully it is gathered and how critically it is appraised, indicates definitely that an ulcer is or is not present, and that, therefore, it would invalidate, to any great degree, the roentgen findings

Ross Golden, M.D. (New York): The officers of the Society and the essayists are to be greatly complimented. Dr. Templeton's discussion of the technic of examination of the stomach impresses me as most desirable. In George Holmes' Caldwell Lecture in 1940, he expressed regret that the programs of our national societies do not include discussions of the technic of x-ray examinations. It would be helpful to all of us if the problem of the technic of gastric examinations could be dealt with as a round-table discussion which would last for an hour or two so that questions could be asked and suggestions could be made.

I agree with Dr. Sosman that antispasmodics are not worth much. When a speaker mentions antispasmodics, he usually means atropine or some form of belladonna, as I understand it. If I am correctly informed, atropine can act on parasympathetic nerve endings which are outside of the reactor cell. Because the nerve endings are within the smooth muscle cell, there would be little probability that atropine could affect the smooth muscle of the stomach. The physiologists believe (I may be wrong about this) that gastric peristalsis is stimulated by the parasympathetic, and that the same stimulus tends to relax the pylorus, whereas sympathetic stimulation tends to cause the pylorus to contract. If this is correct,

it is not logical to give atropine, which blocks the parasympathetic, which is supposed to inhibit the sympathetic and, therefore, to relax the pylorus.

A number of French radiologists are now using injections of morphine as a stimulant to gastric peristalsis. This method, as far as I know, has been used very little, if at all, in this country and may be worthy of further investigation.

With reference to the remark of Dr. Harris concerning the relative importance of fluoroscopy and films, I remember that in 1927 Hans Berg told me that he used fluoroscopy largely as a means for orienting his films. You will remember that Dr. Berg played an important part in the early development of the use of spot films. I was a little surprised to hear him make this remark because fluoroscopy meant more to me than a method of centering films.

I find myself in disagreement with Dr. Morgan on the size of the fluoroscopic screen. I found that, during gastro-intestinal fluoroscopy, my field never exceeded 10 inches in any direction, but of course I never used a 10 × 10-inch field. Sometimes in studying the transverse or the descending colon, a long, narrow field is indicated. Frequently it is desirable to make an 8 × 10-inch spot film. I would be unhappy with a screen as small as he mentioned. Fluoroscopic inspection of the chest should be part of every gastro-intestinal study. It is desirable to have a screen large enough so that the two sides of the diaphragm can be seen at once.

In regard to protection, we now have available lead rubber aprons which come across the lower part of the neck and out over the shoulders and then down the sides. These new aprons give much better protection than anything we have previously had available.

The paper on gastroscopy was also very interesting. Like Dr. Sosman, I would compliment Dr. Dailey on his approach. The gastroscope, like the fluoroscope, is merely an instrument which is no better than the man who is using it. I would like to ask Dr. Dailey whether he has had occasion at any time to try gastroscopy with the patient in the erect position.

In connection with Dr. Wilbur's paper, I would like to point out that any radiologist worth his salt is a clinician. He takes the opportunity during the fluoroscopic examination to ask the patient questions about the character and radiation of pain and other symptoms. The figures presented by Dr. Wilbur do not agree with my impressions concerning the value of the clinical diagnosis of ulcer. My impressions have been gained from the examination of patients and from literally thousands of discussions with good clinicians about case problems.

Thank you for this opportunity to make these comments.

Dr. Bell. If there is no further discussion, I'll give Dr. Harris a chance to defend himself.

Dr. Harris: I think that there is no question that in chest examinations, the detail that is revealed by the film is necessary and that fluoroscopy is of minor importance. However, in gastro-intestinal disease, I believe that there is a group of clinics in this country who have used surgical means to confirm or disprove lesions, both negative and positive, demonstrated by fluoroscopy and have found it very accurate. That is, the fluoroscopic evidence has been very accurate in determining the presence or absence of disease in the stomach and duodenum.

The question comes up, of course, as to the skill of the person using the instrument. I believe that those who can do fluoroscopy well, should use the fluoroscope; those who need spot-film devices, should use them. I don't wish to give the impression that we don't use spot films and don't use routine positions, because we do, but we depend on the fluoroscope, primarily, for the diagnosis.

The duration of the fluoroscopic examination is also important, as Dr. Morgan has said. It should not exceed five minutes for the ordinary complicated case and probably only one to two minutes for the uncomplicated case.

As to the question of antispasmodics, we got into that, too. By that I mean the use of antispasmodics in differentiating a spasm of the antrum from an antral carcinoma. However, those cases are rare. I believe that antispasmodics are indicated. Certainly the question of antral spasm resolves itself into something other than relaxing the patient for five, ten, or twenty minutes, or seeing him the next day.

Dr. Bell: Thank you, Dr. Harris. Dr. Morgan, do you have anything to say?

Dr. Morgan: Dr. Templeton raised the question of the practical advantage of the small focal spot in fluoroscopy. I should like to say at the outset that the data which you saw on the screen this afternoon were not mathematically calculated data but were derived from physiological experiments, the nature of which we do not have time to go into this afternoon. However, they were based on experiments that closely simulate fluoroscopic conditions, and I believe that the curves that you saw actually represent what you may expect when performing fluoroscopic examinations of the gastro-intestinal tract on average patients. Now, you will notice within those curves that the difference between the small focal spot and the large focal spot is particularly marked in the objects of high contrast, and I think that it is rather significant that the images which you see fluoroscopically of the gastro-intestinal tract are images in which the contrast is

approaching 100 per cent. Although at one time I was a little skeptical about the difference in small and large focal spots, the experimental studies indicate that there is a difference.

You will notice that the size of the object in abdominal fluoroscopy at 100 per cent contrast has to be about twice as large for visualization when the focal spot is very large and the object is about 10 cm. away from the screen than when the focal spot is of the order of 1 mm. Not infrequently that is going to be the difference between picking up a small crater and missing it, and I certainly think that one should avail himself of the best possible apparatus, particularly when present-day equipment makes it easy to obtain fluoroscopic tubes of small focal-spot size just as readily as ones with large focal-spot areas.

Dr. Golden raised two questions. One question concerned the size of the screen. We happen to be using an 8 × 10 screen at the present time, although much of our fluoroscopy is done with one of about half that area. I believe that much of the feeling regarding the size of fluoroscopic fields is a matter of personal preference. It is rather interesting to relate one story which I remember from my days at the University of Chicago.

There we had a screen with an area of approximately 28 square inches, but it was possible to hang a regular 12 × 16-in. screen on the fluoroscope with practically no difficulty. It was never a problem of having to unscrew a number of gadgets and go through a lot of other difficult procedures. Well, for the first few days after that fluoroscope went into operation, it was common practice for the fluoroscopists (and that included every member of the group there) to fluoroscope chests with the large screen and then to lift it off and use the smaller screen for other examinations, such as studies of the gastro-intestinal tract. It was rather significant, I believe, that within about one or two weeks the large screen was discarded entirely for chest fluoroscopy and has not been used since. That was back in 1938, and the radiologists there have not felt the need of a large screen following their education in the use of the smaller one.

Dr. Sosman raised a question about protection in fluoroscopy and the new aprons. As he so admirably brought out, it begins to look as though the danger areas of fluoroscopy can probably be taken care of by lead aprons that can be hung on the screen. Suitable small aprons draped about the screen can probably supplant much of the present heavy paraphernalia, and I hope that our future studies will bear this out. Certainly it would be a great boon to every radiologist if he could do away with the cumbersome apron that he now has to put on, when so much of the scattered radiation that comes out of the fluoroscope is concentrated in such a small area. I hope that by this time next year we can report some progress in that direction. At least that is the direction in which we shall be working.

Dr. Bell: Dr. Dailey next, please.

Dr. Dailey: I certainly agree with Dr. Sosman's comments that there is no competition between roentgenology and gastroscopy. In fact, the opposite point of view, although sometimes expressed or implied, is quite ridiculous, because the radiologist is the one who has paved the way for the examination of the gastroscopist and, thus, the cards are all stacked in the latter's favor.

In our last 400 patients, we found only 3 ulcers not suspected radiographically, and these were high behind the ribs so that palpation was not possible. As far as the large rugae are concerned, I do agree with Dr. Sosman as to their correlation with the acidity of the gastric secretion. In any event, it is obvious that to call such a hyperemic mucosa a gastritis is as inappropriate as to say that a man has a dermatitis when he has a red, sweaty forehead from working in the hay field.

Dr. Golden asked if we had examined patients while they were sitting down. Some have done that purely with the idea of trying to visualize the pylorus more satisfactorily. We have done our examinations along the conventional lines.

Dr. Wilbur: One would anticipate, of course, that a clinician would be taken for a ride by a group of radiologists, but I have a few answers for some of the problems which have been brought up.

Dr. Sosman suggested, I believe very wisely, that patients who have symptoms of indigestion should be radiologically examined immediately and not after two or three weeks of treatment. However, I must say that I do not believe that two or three weeks of treatment would make much difference in the results of the examination, because gastric and duodenal ulcers, as a rule, will not heal in that period of time. Recently Cummings, Grossman, and Ivy in studies on the healing time of gastric and duodenal ulcers, as shown by radiological disappearance of the crater, found that the average time of healing of a duodenal ulcer in a group of young men in the Army was approximately forty-two days. Their experience is in agreement with that of other clinicians.

The incidence of carcinoma of the stomach in patients with active duodenal ulcer is a very important problem. I hope that those of you who are working in hospitals with large services will tabulate data on this subject. Some years ago, Dr. Rivers and I reviewed this problem and came to the conclusion, although we could not prove it, that carcinoma of the stomach did not commonly occur in patients who had an active duodenal ulcer. The type of mucosa which is present in the stomach of patients with active duodenal ulcer is probably not the type of mucosa which is suitable soil for the development of carcinoma. That

is not a proved fact, however, and I think that additional data are needed.

Repeated examinations are extremely important, particularly in those patients whom one sees in private practice, and on whom it is not so easy to obtain frequent repeated examinations or follow-up over long periods of time. As far as antispasmodics are concerned, I agree with the majority of the previous speakers. Recently, Dr. Bargen and his associates have shown that, so far as the small bowel and colon are concerned, no antispasmodic, either of the atropine-belladonna series or the synthetic variety, has ordinarily any effect on the musculature of the bowel.

Dr. Golden brought up some interesting problems that I would like to discuss briefly. He mentioned particularly the fact that radiologists commonly ask patients about symptoms, and I've heard a few comments here and there about examinations which last one or two or five minutes. Again, I think that it is a matter of great importance who takes the patient's history. Duodenal ulcer is one of those conditions where, frequently, one can make the diagnosis in the first twenty-five words of history taking. Nevertheless, there are many patients who have a duodenal or gastric ulcer on whom one cannot make the clinical diagnosis on the basis of the history taken in just a few minutes. It is quite true, of course, that there are lesions other than ulcer which will produce the so-called ulcer story: carcinoma of the stomach, gallbladder disease, carcinoma of the pancreas, hookworm disease, etc. However, the clinician will usually find sufficient evidence of these other diseases to put him on guard so far as a diagnosis of ulcer is concerned.

I might also add, since there seems to be some question as to the relative value of fluoroscopy and spot-film examination, that I think the clinician should have his chance to say a word. There is often a disagreement between the clinician and the radiologist following their respective examinations. Under these circumstances, an accurately taken history and repeated radiological examinations are very important. You will recall that my figures showed that in 14 patients for whom x-ray examination was done because of an "ulcer" history, there were only 3 in whom the radiologist reported normal findings. I think that fits in pretty well with what I have just said.

Another important point that all of us are apt to forget is this. When you, as radiologists, make a diagnosis of ulcer, you feel absolutely certain that an ulcer is present; so do I when I take a history of a patient and find a typical ulcer story and nothing else. I feel just as sure as you do that the patient has an ulcer, and yet there is rarely any anatomical evidence that either of us is correct. Even the surgeon, when he operates, may find slight scarring, but he rarely opens the duodenum, or even when he does, it is sometimes difficult for him to tell whether or not an ulcer is present. Unless one has some definite anatomic evidence for it, I think that we should not accept a radiological diagnosis of evidence of ulcer as absolute. Of course, I am vulnerable in exactly the same way, and you can say that one should not absolutely accept a clinical history as evidence of ulcer either.

The point was raised that 10 per cent of all individuals have duodenal or gastric ulcers some time during their lives; that, of course, is true. It explains the fact that in a number of instances the radiologist finds evidence in the duodenum which leads him to suspect ulcer which the clinician will not accept because he is unable to get a story of ulcer symptoms at any time.

Dr. Bell: There have been at least two hands raised in the front row here, and if there is no objection from the audience, I will give Dr. Golden one minute and Dr. Sosman one minute.

Dr. Golden: For the sake of the record, I would like to comment on Dr. Wilbur's remark concerning the duration of fluoroscopy. When a radiologist says that he fluoroscopes a patient for two minutes he does not mean that the patient was in the fluoroscopic room for only two minutes. He means that the total duration of x-ray exposure was two minutes, or five minutes, as the case might be. The patient might be in the fluoroscopic room for as long as ten or fifteen minutes, but would still get less than five minutes of actual exposure during that time. During a fluoroscopic examination, therefore, one has plenty of time to chat with the patient about his symptoms.

Dr. Sosman: There are two points that I would like to make. One is that, in spite of Dr. Harris' statement, I still think that antispasmodics are no good. In fact, I think they are even worse than that; that it is harmful to give a big dose of an antispasmodic, as one may conclude that, if relaxation doesn't occur under this massive dose of antispasmodic, we must be dealing with a carcinoma. I say that we should throw out antispasmodics; don't use them; don't depend on them at all.

Another thing, Dr. Wilbur, the duodenal ulcers often are shallow lesions, and they may heal in ten days. I have seen that happen again and again. Many of them will heal in three weeks. The healing time of the gastric ulcer depends on its size, and we can make a mathematical chart of the size of the ulcer as related to the time that is required for healing *if the patient is under perfect medical control*, and not in one of the Army hospitals, where he may be very unhappy.

Evaluation of the Effects of Radiation on Non-Malignant Lesions of the Nasopharynx[1]

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CROWE (1) CALLED attention to the fact that lymphoid tissue in the nasopharynx, especially the lateral parts, could, as the result of hypertrophy and hyperplasia, cause intermittent or constant blockage of the nasopharyngeal orifices of the eustachian tubes. He noted that such blockage interfered with the normal ventilation of the middle ear cavity and was reflected, most often in children, in decreased hearing. The examination of the ear drums revealed retraction of the tympanic membrane and a reddish blush from the edematous mucosa of the medial wall of the tympanic cavity. Examination with an electric nasopharyngoscope showed actual encroachment of the lymphoid elements on the mouth of the eustachian tube.

It was evident that surgical extirpation of the oral and nasopharyngeal lymphoid structures, no matter how complete, could not reach the laterally placed portions in the fossae of Rosenmüller and about the lips of the tubal orifice without causing serious damage to the mucosa and nearby anatomic parts. Other investigators (2, 3) had previously reported the susceptibility of lymphoid tissue to radiation. Crowe, therefore, with Dr. Curtis F. Burnam, devised a nasal applicator, the end of which contained a compartment enclosing a specified amount of radioactive material, which could easily be passed along the floor of the nose and be applied directly to the area of the nasopharyngeal orifice of the eustachian tube.

In 1946, Crowe (4) reported on a large series of children with tubal obstruction as shown by decreased acuity of hearing, retraction of the tympanic membranes, reddish or cyanotic discoloration of the medial wall mucosa, and encroachment of lymphoid tissue on the orifice of the eustachian tube as demonstrated by the electric nasopharyngoscope. After adenoidectomy to remove the large mass of tissue, irradiation by means of the nasal applicator was used. Hearing improved and the other signs of obstruction disappeared. Similar results were not obtained by adenoidectomy alone.

Crowe (4) also demonstrated the relationship of nasopharyngeal lymphoid tissue to allergic manifestations in the nose and bronchi by obtaining alleviation of allergic symptoms by nasopharyngeal radiation, either with or without previous adenoidectomy. Other investigators have corroborated his findings, both in children with hearing loss secondary to tubal obstruction and in those with evidences of allergy.

Fowler (5) extended Crowe's studies to tubal obstruction in adults. During the war, in a carefully controlled series, he was able to demonstrate that many flyers previously incapacitated for duty because of painful aero-otitis and subsequent hearing loss, could be returned to full flying status after application of radium to the tubal orifices. His microscopic slides revealed the destructive effect of radiation on nasopharyngeal lymphoid tissue.

The series of cases to be presented here represents an attempt at a practical evaluation of what may be accomplished by irradiation according to the method advocated by Crowe (1, 6), as modified by him in January 1947. Certain alterations and added indications are necessarily included to meet our particular office requirements.

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CASE GROUPS AND INDICATIONS

This series includes 50 patients who have been followed carefully at the office for a year (March 1947 to March 1948). The cases were divided into four main groups, in the hope of finding the group or groups in which the best results from radiation might be expected.

Group I: Thirteen cases of well defined or fixed otologic impairment, either nerve deafness or conductive deafness (the latter otosclerotic or adhesive in character), constituted the first group. Irradiation of the nasopharynx in these cases was used in order to throw light on any possible added detrimental influence that lymphoid tissue about the orifice of the eustachian tubes might have.

In 9 patients (6 children, from three and a half to eleven years, and 3 adults) nerve deafness of a handicapping degree (below 30 decibels) was present. Audiometric tests in this group, before and after irradiation, showed no evidence of improvement in hearing. In the remaining 4 cases, a significant amount of adenoid tissue was present. Two of these patients were young girls, fourteen and seventeen years old, with otosclerosis. Following therapy, one showed a plus 12, plus 6 decibel gain; the other a plus 10, plus 14 decibel gain, but this borderline effect was hardly to be considered of any real value. In the other 2 patients, adults with established adhesive otitis, there was subjective improvement, but audiometrically this could not be demonstrated.

Group II: This group comprised our largest number of cases, 25. It consisted largely of children, with only 2 young adults, aged eighteen and twenty-one. The children's ages averaged from four to nine years. An outstanding feature was the tendency to allergy and the frequency of an allergic family background. The most important symptoms were difficult nasal breathing, recurrent earaches, frequent sore throats, hoarseness, secondary nasal infections following colds, mouth breathing, and coughing. Physical findings included pallor and bogginess of the nasal mucosa, reddish blush from the medial wall mucosa, infection of lateral bands of the pharynx, abundant lymphoid follicles on the posterior pharyngeal wall, and, on palpation, lymphoid masses of significant size in the nasopharynx. All had had tonsils and adenoids removed and in all some definite allergic background was present.

Deafness or recurrent episodes of deafness did not seem to be factors in this group. In 23 of the 25 cases, there was considerable improvement of symptoms over a period of two to four months. (We do not anticipate complete alleviation of symptoms.) It is possible that the improvement of nasal and eustachian tube ventilation prevents the occurrence of future hearing loss. We combine radiation therapy with other methods of managing the allergic child in otolaryngologic practice.

Group III: The third group comprised 8 patients, 7 adults (ages thirty to fifty) and a child of eight years. Symptoms in these cases were "clicking" noises in the ears, tinnitus of other types, intermittent "stopped up" sensations in the ears—all of which suggested eustachian tube obstruction. As in group II, hearing loss was not a feature. Four of the 8 patients mentioned that some of their symptoms were improved following completion of irradiation. The other patients were unable to report any remarkable change.

Group IV: The last group consisted of 3 cases of chronic aural discharge. It was hoped that relief of eustachian tube obstruction would lead to restoration of normal physiology, with resultant diminution in discharge or "dry ear." Following irradiation, however, there was no change in the character or amount of discharge.

COMMENT AND CONCLUSIONS

1. In our hands, irradiation has been useful when combined with other forms of therapy in the child with a syndrome of impaired hearing of transitory character and allergic symptoms, *i.e.*, difficult nasal

breathing, postnasal drainage, sneezing, coughing, otalgia, and mouth breathing. Associated paranasal infections were invariably present.

2. The effects noted in those cases with fixed impairment of hearing of obvious otologic cause (otosclerosis, adhesive otitis media, nerve deafness) have been disappointing, but not unexpectedly so.

3. In mild disturbances of eustachian tube function, radiation may be of value. More cases and further experience will be necessary to assay its full benefit in these instances.

4. The experiences of Scal (8), Boies (9), Fricke and Brown (10), Harris and Montgomery (11), and Gay (12), have followed a similar pattern.

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SUMARIO

Valuación de los Efectos de la Irradiación en las Lesiones No Malignas de la Nasofaringe

En una serie de 50 casos que comprendían tanto niños como adultos, utilizóse la irradiación de la nasofaringe con el aplicador de radio introducido por Crowe. El procedimiento resultó útil, combinado con otras terapéuticas, en los niños afectados por un síndrome de audición defectuosa pasajera y manifestaciones alérgicas, es decir, dificultad para respirar por la nariz, escurrimiento postnasal, estornudos, tos, otalgia y respiración por la boca. En esos casos hubo invariablemente infecciones paranasales asociadas.

Los enfermos con insuficiencia auditiva fija de manifiesta etiología ótica (otoesclerosis, otitis media adhesiva y sordera debida a afección del nervio auditivo) no se beneficiaron mayor cosa.

En un grupillo de pacientes con trastornos leves, como zumbidos y sensación de "oídos tapados," que indicaban oclusión de la trompa de Eustaquio, el resultado fué dudoso, pero parece que la irradiación puede ser de algún valor en esos casos.

Tres enfermos con otorrea crónica fueron tratados sin resultado.

Las observaciones anteriores convienen con las de otros autores.

Endocrine Factors in Hypertension; Treatment by Roentgen Irradiation of the Pituitary and Adrenal Regions[1]

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IN A PAPER PUBLISHED in 1933 it was pointed out by one of the present authors (1) that hypertension and diabetes are similar in so many respects as to suggest a least common denominator among their etiologic factors. Evidence available at that time pointing to endocrine participation in these conditions indicated (*a*) that the pituitary and adrenals are probably chiefly involved; (*b*) that an associated hypertension or diabetes, or both, has been found in every variety of hyperpituitarism —gigantism, acromegaly, and basophilism —while hypopituitarism is accompanied by lowered blood pressure and an increased tolerance for glucose; (*c*) that adrenal tumors are often accompanied by hypertension or diabetes, or both, while Addison's disease is characterized by hypotension and hypoglycemia.

That hyperthyroidism may play a role in some cases of hypertension, which show improvement when the thyroid condition is corrected, has subsequently been suggested (2).

Since 1933, additional evidence has accumulated tending to strengthen the belief that the pituitary and adrenals play some part in hypertension and diabetes. This evidence may be summarized as follows: Diabetes has been produced in the dog by intraperitoneal injections of anterior pituitary extracts (3). In rats, hypertension has been produced by intraperitoneal (4) and intrathecal (5) injections of posterior pituitary extracts, and cardiac hypertrophy and nephrosclerosis have been produced by overdosage of desoxycorticosterone acetate and sodium chloride (6). Unilateral adrenal ischemia brought about by subtotal ligation of periadrenal blood vessels causes a prompt and sustained hypertension (7).

MATERIAL FOR PRESENT STUDY

The present study is based on 795 patients with hypertension: 486 of these were seen by one or more of our group, whose names appear above, and 309 were reported to us by other workers. We have seen, also, 42 patients who had both hypertension and diabetes, but these are not included in this report. Some of the patients were employees of the Illinois Central Railroad and had been under observation and treatment by the hospital department for one to fifteen years. The others were encountered in private practice. All were known to have had hypertension for one year or longer and in most the systolic blood pressure was well above 160.

Preliminary studies were intended to be sufficient to establish a diagnosis of essential hypertension. Four patients with nephritis were accepted for treatment; but in only one of these was any improvement noted.

Practically all patients, except those treated by thyroid and pituitary extracts, were within normal limits as to height and weight. The hypercholesterolemia (8) and hypocalcemia (9) reported by others have not been observed in this series. Deviations of the blood sugar were the most significant findings in blood chemistry determinations. Results of glucose tolerance tests in 228 cases were as shown in Table I.

[1] Accepted for publication in April 1948.

None of these patients was considered to have diabetes.

TABLE I: GLUCOSE TOLERANCE TESTS IN 228 PATIENTS

Blood Sugar Levels	Cases	Cases with Glycosuria
Less than 170 mg.%	97	9
170–200 mg.%	54	14
Over 200 mg.%	77	32
TOTAL	228	55

Results of basal metabolism determinations in 183 cases were as follows:

−5 or lower.....53 cases
−5 to +10.....69 cases
+10 or higher.....61 cases

ENDOCRINE ASPECTS OF THE STUDY

In no case has there seemed to be a thymic or parathyroid fault.

Gonads: The administration of estrogenic preparations in doses sufficient to relieve the menopausal symptoms of women did not materially affect their blood pressure. In 3 patients the hypertension was believed to be associated with the male climacteric. All were given 25 mg. of testosterone propionate twice weekly. One case responded favorably.

Thyroid: In 6 patients the hypertension was associated with hypothyroidism; but none of these had myxedema. The basal metabolism rate before treatment varied from −10 to −20. The administration of thyroid in adequate doses in these cases was accompanied by a substantial decline in blood pressure. The dose was kept at that level which would relieve the symptoms without causing tachycardia, heart consciousness, nervousness, or tremor of the outstretched fingers. The basal metabolism rate was not often checked after the preliminary determination.

The following case history is illustrative of the type of response to thyroid therapy in these hypothyroid cases.

A 54-year-old man was first seen on April 18, 1922, complaining of backache and fatigue. He was 30 pounds overweight, the excess being distributed in what was then regarded as a thyroid pattern. The basal metabolism rate was −15; the blood pressure 175/115; weight 184 pounds. Treatment consisted at first of 3 grains of thyroid daily (a Burroughs Wellcome & Co. preparation standardized according to the British Pharmacopeia), with a gradual increase in the dose to 2 1/2 grains four times daily. On Sept. 1, 1922, the patient's weight was 152 pounds, his blood pressure 125/80, and his pulse 90. On March 7, 1923, the blood pressure was 140/90 and the pulse 72, and the dosage of thyroid was reduced to 2 1/2 grains three times daily.

The patient was next seen on July 9, 1927, when the pulse was 66, blood pressure 220/105, weight 177 pounds. He had taken no thyroid for several years. He was again given thyroid, 2 1/2 grains three times a day. Observations during the next ten years were as shown in the accompanying table.

When the patient returned to the office after a long absence he usually reported that he had discontinued the thyroid several months before his visit. He is said to have died of a stroke in 1945.

Three patients with hyperthyroidism were treated by irradiation of the pituitary and adrenal regions. Their response is illustrated by the following case.

PULSE AND BLOOD PRESSURE DETERMINATIONS IN A HYPOTHYROID PATIENT RECEIVING THYROID THERAPY, AUG. 30, 1927–MARCH 6, 1937

Date	Pulse	Blood Pressure	Weight	Thyroid Dosage
Aug. 30, 1927	77	155/80	155½ lb.	....
Jan. 17, 1928	66	155/80	...	2½ gr. × 4
June 8, 1929	66	165/76	...	2½ gr. × 1
Oct. 21, 1929	..	140/70	...	1 gr. × 3
Feb. 10, 1930	75	180/85	...	1 gr. × 3
July 11, 1930	80	120/60	...	....
March 2, 1931	64	180/90	...	1 gr. × 3
March 30, 1931	..	140/80	...	....
May 23, 1932	..	165/90	...	1 gr. × 3
June 19, 1932	80	150/75	...	....
Nov. 17, 1933	72	220/100	165 lb.	2½ gr. × 3
Dec. 1, 1933	84	175/80	...	2½ gr. × 2
Aug. 24, 1934	60	165/85	156 lb.	2½ gr. × 3
June 3, 1935	70	155/75	...	2 gr. (U.S.P.) × 1
March 6, 1937	66	160/80	...	2 gr. (U.S.P.) × 1

A woman with recurrent hyperthyroidism, who had undergone two subtotal thyroidectomies and was scheduled for a third because of a large mass of thyroid tissue, was taking Lugol's solution when she came under observation. The medication was continued and x-ray therapy was added. After six treatments of 50 to 55 r over each of three areas, the right and left pituitary and both adrenals (120 kv., 2 mm. Al filter, 5 ma., 50 cm. distance) at weekly intervals, the blood pressure dropped from 205/75 to 135/75 and the basal metabolism rate from +56 to +18. All symptoms were relieved except those due to an already irreparably damaged heart. Seventeen months after the last x-ray treatment the blood pressure was 155/90 and the basal metabolism rate +14. The mass of thyroid tissue was apparently unchanged.

McGregor (10) reported satisfactory results in his efforts to prevent postoperative hyperthyroid crises by preoperative irradiation of the pituitary and adrenal regions, using the same technic which we employed in the treatment of hypertension.

In this connection it should be pointed out that the role of the thyroid in hypothyroidism is well understood and that in its severe form, as myxedema, hypothyroidism may produce a picture resembling nephritis; on the other hand, our understanding of the exact role of the thyroid in hyperthyroidism is still incomplete.

Adrenals: Adrenal biopsies were done in two female patients and no adenomata were found. Small ones were found in a third patient postmortem, too small to have been recognized except on surgical exploration. The history of this patient follows.

The patient was first seen on Sept. 9, 1934, when she was 34 years of age. She complained of irritability, shortness of breath, and precordial distress. Her temperature was 99.6°, pulse 100, blood pressure 260/145. She had known that she had hypertension for four years. Her eyes were prominent, suggesting exophthalmos, and the conjunctivae were injected. There was an excessive amount of hair over the body and face. The basal metabolism rate was −5.

Irradiation was given to the pituitary and adrenals. Between Sept. 17 and Dec. 7, 1934, the pituitary region received 1,460 r and the adrenal region 777 r, measured in air. Symptoms were relieved, and the blood pressure decreased to 220/145 right and 195/135 left.

The patient was next seen on Dec. 31, 1935, when her blood pressure was 250/160 and basal metabolism determinations, reported from another hospital were +55 and +35. She complained of headache, palpitation, and dyspnea, and was disoriented at times. X-ray treatment produced a drop of 20 mm. in blood pressure, lasting about twenty-four hours. Death occurred Jan. 15, 1936, of myocardial failure. Postmortem examination showed hypertrophy of the heart, nephritis, hyperplasia of the hypophysis and thyroid, and adenomata in both adrenals.

Another case was followed from 1936 to 1948.

A 60-year-old widow came under observation on Feb. 26, 1936. She had known that she had hypertension, she said, for seven years. She also had a glaucoma and in earlier years had a bleeding duodenal ulcer, which continued to flare up occasionally. Her first blood pressure reading was 220/130. She was given x-ray treatment two to six times a year, with the same technic and dosage already described—50 r to each of three areas (two pituitary and one adrenal). The first three blood pressure readings were as follows:

Feb. 28, 1936	175/110
March 7, 1936	160/110
April 4, 1936	155/90

The blood pressure readings at approximately one-year intervals, together with the dates of the x-ray treatments in each of these years are shown in the accompanying table. The blood pressure was sometimes higher and sometimes lower than on the dates recorded:

Date	Blood Pressure	X-ray Treatment (three areas), 50 r each
Feb. 3, 1937		X-ray treatment
April 9, 1937	160/90	
June 2, 1937		X-ray treatment
Feb. 14, 1938		X-ray treatment
Feb. 21, 1938		X-ray treatment
April 9, 1938	160/95	
June 26, 1938		X-ray treatment
Sept. 14, 1938		X-ray treatment
Feb. 10, 1939		X-ray treatment
April 12, 1939	160/95	
Sept. 9, 1939		X-ray treatment
Sept. 22, 1939		X-ray treatment
Oct. 14, 1939		X-ray treatment
Nov. 10, 1939		X-ray treatment
Jan. 12, 1940		X-ray treatment
April 17, 1940	160/95	X-ray treatment
Aug. 10, 1940		X-ray treatment
Aug. 19, 1940		X-ray treatment
Nov. 30, 1940		X-ray treatment
Dec. 31, 1940		X-ray treatment
Jan. 27, 1941		X-ray treatment
Feb. 5, 1941		X-ray treatment
March 31, 1941		X-ray treatment
April 19, 1941	180/105	
April 21, 1941		X-ray treatment
May 10, 1941		X-ray treatment
Sept. 29, 1941		X-ray treatment
Jan. 19, 1942		X-ray treatment
April 20, 1942	165/110	

May 18, 1942		X-ray treatment
Aug. 25, 1942		X-ray treatment
Oct. 3, 1942		X-ray treatment
Nov. 6, 1942		X-ray treatment
Dec. 21, 1942		X-ray treatment
Feb. 27, 1943		X-ray treatment
April 19, 1943	160/110	
July 8, 1943		X-ray treatment
Aug. 26, 1943		X-ray treatment
Oct. 7, 1943		X-ray treatment
Jan. 19, 1944		X-ray treatment
Feb. 24, 1944		X-ray treatment
April 17, 1944	165/95	
May 11, 1944		X-ray treatment
Nov. 11, 1944		X-ray treatment
Nov. 24, 1944		X-ray treatment
April 14, 1945		X-ray treatment
April 15, 1945	165/100	
Nov. 1, 1945		X-ray treatment
Jan. 19, 1946		X-ray treatment
April 30, 1946	170/105	
Aug. 30, 1946		X-ray treatment
April 11, 1947	180/90	
May 15, 1947		X-ray treatment
Nov. 5, 1947		X-ray treatment
April 7, 1948	170/100	

Fifteen patients (2 men and 13 women) were obese, middle-aged, and thought to have pituitary-thyroid deficiency. All but one were put on a diet of 1,200 calories (carbohydrate 80, protein 80, fat 40 gm.). All were given thyroid in tolerance doses (2 grains per day was the usual dose), and all received injections twice weekly of 0.5 c.c. of anterior pituitary extract[2] and 0.5 c.c. of posterior lobe extract, representing 5 units. These were given in the same syringe at the same time. One man and 10 women showed significant improvement. The history of the first of this group is as follows:

An Illinois Central locomotive engineer, aged 62 years, was admitted to the hospital because of dyspnea, swelling of the feet for three years, and pain and swelling of the abdomen for one year. He complained also of vertigo and headache for the past few months, and of marked diurnal somnolence. He weighed 222 pounds. Heart tones were distant, and a systolic murmur was heard over the aortic area. There was pitting edema to the knees. The liver was tender and a ventral hernia was present. Blood pressure was 186/90. There was a trace of albumin in the urine. Blood uric acid was 5.5 mg. per cent, cholesterol 195 mg. per cent, the basal metabolism rate −9.

The patient's trouble was considered to be due to cardiac insufficiency and he was treated by bed rest low-calorie diet, and digitalis, without effect. Because of the obesity, dry skin, brittle nails, and other signs of thyroid and pituitary deficiency, an endocrine component was suspected. In spite of the hypertension, the patient was given 5 units of a posterior pituitary extract and his blood pressure checked thereafter at fifteen-minute intervals for one hour. It dropped from 184/84 to 144/60. The following day an injection of 0.5 c.c. anterior pituitary extract had a similar effect. Both extracts were then given twice weekly, with 1 grain of thyroid per day. On that regime the blood pressure dropped to 125/80, and the edema and other symptoms disappeared, and there was a loss of 35 pounds in weight. The patient was still in good health at the time of his retirement from service some years later.

Only obese patients who show signs of thyroid and pituitary deficiency are considered as candidates for this treatment, and their reaction to these extracts is tested out before any treatment is given. That is, the patients are given one extract on one day and the other on another, and their blood pressure response is checked at fifteen-minute intervals for an hour or more. Unless the blood pressure shows a marked drop, no further injections are given.

We realize that the treatment of these 15 patients seems to be in conflict with statements made in the opening paragraphs, and we offer no explanation of the mechanism. Griffith *et al.* (11) recently reported on the use of pitressin in hypertension and suggested that injections of this preparation led to the formation of antihormones which reduced the output of pituitary hormones. We do not feel that this was true in the cases here reported, because the fall in blood pressure occurred so promptly after the injection.

Seven patients (5 women and 2 men) were thought to show evidence of anterior lobe deficiency, the most obvious features being short stature, delicate osseous development, and a basal metabolism rate below normal. All were given small doses of thyroid daily and 0.5 c.c. of anterior pituitary extract twice weekly. Five (4 women and 1 man) showed significant improvement of symptoms and fall in blood pressure. The following case history indicates the type of case and its response.

[2] Anterior Pituitary Extract (Parke, Davis & Co.) formerly marketed as Antuitrin.

A 48-year-old man reported that he had been found to have hypertension three years before. It had produced no symptoms. He was 5 feet 7 1/2 inches in height and weighed 179 pounds, and his face was suggestive of acromegaly. Roentgenograms of the sella showed the longest diameter to be 13 mm., but there was no sign of erosion of the clinoid processes or sellar floor. The blood pressure was 155/100. Physical examination was otherwise negative. The basal metabolism rate was −16. An injection of 0.5 c.c. of anterior pituitary extract was followed by a fall in blood pressure to 130/95. The injections were continued once a week, plus 1/2 grain of thyroid per day. The blood pressure fell to 120/80.

In this group of cases, also, we are at a loss to explain the mechanism of the fall in blood pressure. All patients showing evidence of growth hormone deficiency are tested for their response to anterior pituitary extract. If a pronounced fall in blood pressure occurs within an hour after the injection of 0.5 c.c., it is considered likely that the patient will be benefited by a course of such injections given twice weekly. Obviously, such cases are not common, as we have encountered only 7 such patients in a series of 486.

Of the 12 physicians in our series, 3 were treated surgically as well as by x-ray. One was under irregular observation and treatment for about one year, during which he was symptomatically improved and his blood pressure was maintained at about 180/120. It rose, soon after treatment was discontinued, to its pretreatment level of 240/140 and bilateral splanchnicectomy was done. Immediately after the operation, the symptoms practically disappeared and the blood pressure fell to nearly normal figures. This lasted about four months, when symptoms recurred, the blood pressure again rose to approximately its preoperative level, and death ensued shortly thereafter from cerebral hemorrhage.

The second physician experienced some symptomatic relief and his blood pressure fell almost to normal. After about six months, however, symptoms returned and the blood pressure rose to approximately its preoperative level. Irradiation had no effect on either symptoms or blood pressure. Death ensued from renal insufficiency.

In the third case symptomatic relief lasted about three years. The patient did not know when his hypertension recurred. One x-ray treatment relieved the symptoms but had little effect on the blood pressure.

Two other patients have undergone surgical as well as x-ray treatment. The history of one of these follows:

Mr. T. was admitted to the hospital in 1929 at the age of 27 because of recurrent glomerulonephritis which had attacked him first in 1919. About the middle of 1932 he was seen in the Out-Patient Department for hypertension. His blood pressure was then 170/110. In February 1934 it was 165/110. After four x-ray treatments, it dropped to 145/105, and the patient was symptomatically improved. In February 1937, he was admitted to the hospital because of headache, vertigo, and failing vision due to retinal hemorrhages and papillary edema. His blood pressure was 240/180 and a renal function test showed the phenolsulfonphthalein output to be only 40 per cent. In May 1937 he underwent bilateral splanchnicectomy, and the systolic blood pressure is said to have dropped from 260 to 180 (the diastolic was not reported). He was practically symptom-free until September 1942, when he again complained of failing vision and the blood pressure had risen to 205/140. He was admitted to the hospital for hemorrhages in the eye associated with hypertension, and while there contracted pneumonia, following recovery from which he was discharged for a long rest.

In May 1943, headache recurred and the blood pressure was 210/130. The patient's chief complaint, however, was bilateral gynecomastia, which became quiescent after a course of injections of chorionic gonadotropin and testosterone propionate. The blood pressure response to that treatment, which was not given by us, is not recorded.

The patient was again seen in June 1944, because of headache and vertigo. The blood pressure was 190/130. It dropped, after x-ray treatment, to 155/105 and symptoms improved. The blood pressure was maintained at about 160/100 by further x-ray treatments on June 19 and 26, Aug. 2, and Oct. 27, 1944, but had risen to 190/130 in February 1946. X-ray treatment was again given, and the blood pressure again dropped to 160/110, at which figure it has been maintained by repeated irradiation (Feb. 11 and 25, March 11, and Aug. 19 and 26, 1946). The patient remains almost free of symptoms.

RATIONALE OF X-RAY TREATMENT

Since 1914 unsuccessful attempts have been made to reduce the blood pressure of hypertensive patients by irradiation of the

adrenals. Raab (12) reported relief of angina pectoris by this means, though the blood pressure was not significantly affected. Irradiation of the pituitary is said to have caused considerable improvement in selected cases of hypertension (13, 14). So far as we know, however, we were the first to attempt to combine irradiation of the pituitary and adrenal regions with small doses of x-ray in the treatment of this condition.

A number of theories may be advanced to explain the phenomena noted in this report. It is possible that small doses of x-ray have a regulatory effect on pituitary function, changing the proportion of the various hormones elaborated. The same dose, for instance, is effective in various menstrual disorders. A similar regulatory effect may be true of the adrenals. If the kidney elaborates a pressor or antipressor substance, one might be increased or the other decreased by the rays.

Since the effects seen following irradiation of the pituitary and adrenal regions are so similar to those reported as following sympathectomy, it may be that the effects of irradiation are mediated through the sympathetic system.

TECHNIC AND RESULTS OF TREATMENT OF HYPERTENSION BY X-RAYS

Four hundred and thirteen patients with essential hypertension were treated by small doses of x-rays to the regions of the pituitary and adrenals.

Dosage, Technic, and Precautions: As this was a new venture and we wished to be on the safe side, we began with very small doses of radiation. The first case was followed for one year before a second was accepted for treatment. Later we gradually increased the dose, but found that when more than 100 r was applied to each area, worth-while results were not obtained.

The factors we have found most satisfactory are: 120 kv., 3 mm. aluminum filter, 50 cm. skin-target distance, 3–5 ma. About 50 r, measured in air, are delivered to each area treated. Irradiation is applied to three areas at each sitting—to both sides of the pituitary through a 10 × 10 cm. portal and to the adrenals through a common portal 15 × 15 cm.

We do not know that this is the ideal dose, nor do we know whether the dose should be varied from one patient to another or in the same patient at different times. Our experience with heavier doses has already been mentioned. Other workers using higher dosage have reported them as without satisfactory effects (15).

We cannot explain why small doses should produce good results when larger ones fail. This, however, is not an unusual observation. Others have discussed these phenomena (16). Small doses of x-rays are beneficial in the treatment of certain infections, where larger doses are ineffective. The same thing is observed in the action of some drugs (20).

The blood pressure should be checked at intervals of three to seven days, particularly after the first treatment. *If symptomatic relief and a marked fall in blood pressure occur, no further treatment should be given until the blood pressure rises or symptoms recur.* One or two treatments are thus sufficient in some cases for several months. If no such favorable reaction occurs after the first treatment, another is given about one week later and treatments are then given at weekly intervals until a total of six have been given, provided a favorable response does not occur sooner. *Whenever a marked fall in blood pressure or relief of symptoms occurs—whether it be after the first or some subsequent treatment—treatment is discontinued until there is a rise in blood pressure or a recurrence of symptoms.*

Presumably a greater number than six of these treatments could be given in one series, but in order to be conservative we have arbitrarily limited the number to six. After an interval of six weeks, another series of treatments may be given if needed.

Results: The results of treatment are shown in Table II. A patient was considered improved when there was a fall

of at least 30 mm. systolic and 10 mm. diastolic pressure, along with symptomatic relief.

TABLE II: RESULTS OF TREATMENT

Adequately treated (3 or more treatments)		
Improved	231	(70.4%)
Unimproved	97	(29.6%)
Total	328	
Inadequately treated	60	
Not followed	25	
Total	85	
Cases reported by others		
Improved	238	(77.0%)
Unimproved	71	(23.0%)
Total	309	
Grand total	722	

As appears from this tabulation, 413 patients received small doses of roentgen rays, according to the technic outlined above, with relief of symptoms and a fall in systolic blood pressure of 30 mm. or more in 70 per cent of those adequately treated. When further treatment was needed, heavier doses were applied. These doses were without beneficial effect on symptoms or blood pressure. After waiting six weeks, treatment was again resumed with small doses, and again the same beneficial result as originally noted was seen.

Three patients who responded favorably to small doses, when further therapy was needed were given a placebo treatment, which was without effect. The use of the small doses of radiation at a later date again proved effective.

Two roentgenologists, in cities twenty-five miles apart, used this method of treatment. One used the small doses we employed and reported that his results duplicated our own. The other used larger doses and reported no effect on blood pressure or symptoms.

In many instances in our series the blood pressure dropped shortly after the first treatment. In some the systolic pressure was lowered 40 to 60 points, while the diastolic remained unchanged. In others the diastolic showed the greater reduction.

Symptomatic relief is usually more striking than the drop in blood pressure and often occurs when the blood pressure is scarcely affected. Furthermore, many patients who experience a fall in blood pressure and symptomatic relief do not have a recurrence of symptoms when the blood pressure returns to pretreatment levels. The symptoms most often and most promptly relieved are headache, vertigo, nervous tension, irritability, heart consciousness, precordial distress, and insomnia. Headache and vertigo often disappear while the patient is receiving the first treatment.

An example of relief from precordial distress is furnished by the case of a thirty-seven-year-old woman who had known of her hypertension for one year and experienced frequent attacks of substernal distress. From April to October 1944 she took 650 glyceryl trinitrate tablets to relieve these attacks. An x-ray treatment was given Nov. 1, 1944 and from then to May 10, 1945 she required only three tablets.

Duration of Effects: Relief of symptoms and reduction in blood pressure last for variable periods of time in different patients and even in the same patient at different times. Some respond favorably for only a short time. These patients complained of headache following the first treatment. In those cases no further x-ray treatment was given. In a large percentage of the patients, by checking symptoms and blood pressure weekly and repeating the treatment as needed, symptoms can be controlled and the blood pressure maintained at substantially lower levels over a period of years. Eventually patients seem to become resistant to treatment. After a period of years—six to eight in our experience—the blood pressure rises even in those who originally responded favorably, and is uninfluenced by further x-ray irradiation, while the symptoms are less strikingly relieved.

We do not know that this treatment prolongs life, though it does in many cases prolong the working ability of these sufferers and makes them much more comfortable.

Comment: Other structures about the pituitary and adrenals are, of course, exposed to the same rays, and changes

wrought in these structures may contribute something to the phenomena we have observed. Langer (17) called attention to certain diseases that responded favorably to irradiation of the vegetative system. It is likely that the autonomic system played a considerable part in producing the results that followed these treatments.

Efforts were made to guard against the influence of psychotherapy. While it is unlikely that we were completely successful in this respect, we do not believe that it played an important role.

As to controls, the fact that many of these patients had already been under orthodox forms of treatment for one to ten years without relief is, in itself, a control. Two patients receiving thiocyanate therapy with little or no effect on either blood pressure or symptoms noted striking and immedately favorable effects on blood pressure when x-ray therapy was added. The cyanates were later withdrawn but the good effects continued.

Three patients have been given x-ray treatments to other parts of the body without effect on symptoms or blood pressure. These were then given treatment to the pituitary and adrenal regions with small doses of x-ray. Prompt relief of symptoms and reduction of blood pressure resulted. The fact that the adrenal region has been irradiated many times and by many workers over the past thirty odd years without significant effect on the blood pressure of hypertensive patients is perhaps the best answer to the suggestion that the effects we have noted have been due to the general biologic effect of the rays and would have occurred if other parts of the body had been irradiated.

It has been suggested that x-ray treatment be tried before surgical intervention (18) and that it might be used as a prophylactic measure in patients in whom hypertension seems likely to develop (19). We have found it helpful in patients with hypertension recurring after surgical treatment. We have failed to obtain improvement in any case of hypertension in the malignant phase.

Irradiation for hypertension is, then, a simple and safe procedure which can be employed wherever proper x-ray equipment is available. For better than fourteen years we have followed more than 400 cases and have never seen the slightest evidence of x-ray damage to any organ or tissue. Biopsy of the adrenals has revealed no sign of damage. Postmortem examination was done in two cases, both of which had received much more irradiation than is now recommended. In neither case was there any damage to the pituitary or adrenals or to any other organ or tissue. At no time have we noted any conflict with any other form of therapy.

SUMMARY

It is believed that at least a small proportion of cases of hypertension have an endocrine background and that every patient suffering from this disorder should have the benefit of an endocrine study.

A series of 795 cases accumulated since 1932 has been studied from this point of view, and cases benefited by various forms of endocrine therapy are reported.

The pituitary and adrenals seem to be most often involved, and x-ray irradiation has been directed to these regions in an attempt to control symptoms and lower the blood pressure. The authors have themselves treated 413 patients, with improvement (a lowering of blood pressure of at least 30 mm. systolic and 10 mm. diastolic, with symptomatic relief) in 70 per cent of those receiving adequate treatment.

The factors which have been found most satisfactory are 120 kv., 3 to 5 ma., 3.0 mm. Al filtration, and 50 cm. target skin distance. Irradiation is applied to three areas at each sitting, two pituitary portals, each 10 × 10 cm., and a 15 × 15 cm. portal over the adrenals, about 50 r, measured in air, being given to each portal. The blood pressure is checked repeatedly following treatment, and irradiation is repeated only when there is no favorable response to the first treatment or there is recurrence of symptoms or a rise in pres-

sure. As many as six treatments may be given in a series, at weekly intervals, and the series may be repeated as needed. Eventually, however, the treatment ceases to be effective (after six to eight years in the authors' experience).

No evidence of x-ray damage has ever been observed following this treatment, and in two cases postmortem study has revealed no injury to the pituitary, adrenals, or other tissues or organs.

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SUMARIO

Los Factores Endocrinos en la Hipertensión: Tratamiento con los Rayos X de las Regiones Hipofisaria y Adrenal

Parece que por lo menos una pequeña proporción de los casos de hipertensión se asientan en un fondo endocrino y que todo enfermo que padezca de dicho trastorno debería disfrutar del beneficio de un estudio endocrinológico. Una serie de 795 casos acumulados desde 1932 ha sido estudiada desde ese punto de vista, y aquí se comunican los beneficiados con varias formas de endocrinoterapia.

La pituitaria y las adrenales parecen ser las afectadas más a menudo y los rayos X han sido asestados a esas regiones con mira a cohibir los síntomas y rebajar la tensión sanguínea. Los AA. mismos han tratado 413 enfermos, con mejoría (baja de la tensión sanguínea por lo menos de 30 mm. en la sistólica y 10 mm. en la diastólica, con alivio sintomático) en 70 por ciento de los que recibieron tratamiento adecuado.

Los factores que resultaron más satisfactorios fueron: 120 kv., 3 a 5 ma., filtración por 3.0 mm. de Al y distancia foco-piel de 50 cm. La irradiación se aplica a tres zonas

en cada sesión: dos puertas, cada una de 10 × 10 cm., en la hipófisis, y una de 15 × 15 cm. sobre las adrenales; cada puerta recibe unos 50 r, medidos al aire. La presión sanguínea es determinada repetidamente después del tratamiento, y sólo se repite la irradiación si no hay respuesta favorable al primer tratamiento o si hay recurrencia de síntomas o alza de la tensión. Pueden administrarse en una serie hasta seis tratamientos a plazos semanales, repitiéndose la serie según se necesite. Sin embargo, con el tiempo el tratamiento deja de ser eficaz (al cabo de seis a ocho años en la casuística de los AA.)

No se han observado jamás signos de lesión roentgenológica a continuación del tratamiento, y en dos casos la autopsia no reveló lesión de la pituitaria, adrenales o de otros tejidos u órganos.

A Rapid Quantitative Scale Method for Estimating the Percentage Concentration of Priodax in the Gallbladder[1]

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EVALUATION OF THE concentration of Priodax (brand of iodoalphionic acid) in the gallbladder during cholecystography has, up to the present time, been subject to variations incidental to different roentgen technics and the personal equation of the interpreter, all other conditions remaining equal. This paper reports a method which automatically eliminates these two variables and equalizes the results of Priodax cholecystography irrespective of technical factors and personal variations.

This is accomplished by use of a stepped scale[2] previously standardized against varying percentage concentrations of Priodax, beginning with the highest concentration possible and ending with the smallest concentration visible to the eye: in other words, the use of a simple, direct-reading five-step scale of known density variations, with which the opacified gallbladder image can be compared directly on the film. The thickness of the matching step obviously increases with the increase of dye concentration.

Radiography is a study of contrasts in density. Since, ordinarily, the normal gallbladder cannot be differentiated from its surrounding tissues, a method for enhancing its contrast had to be devised. This was originally done by Graham and Cole (1) in 1924, with the aid of tetrabromphenolphthalein, which they injected intravenously. This procedure embodied an entirely new and original radiological principle, *i.e.*, utilization of the specific functions of a system to engender a difference in density. Cholecystography is, therefore, largely a test of physiological capacity.

Small variations in the opacified gallbladder as to size, shape, position, and capacity are unimportant if the organ is well visualized, shows a progressively intense opacification, is capable of altering in size, and empties after the administration of a fat-containing meal.

Priodax is beta(4-hydroxy-3,5-diiodophenyl)-alpha-phenylpropionic acid. At the present time it is the product of choice for cholecystography, since it possesses the following advantages: Attendant nausea, griping, and diarrhea, when present, are usually mild. Vomiting is uncommon. There is less patient resistance; the medium is readily accepted and is simple to administer. It is readily absorbed from the gastro-intestinal tract, affording freedom from confusing opacification of the colon due to non-absorbed dye. The number of repeat or confirmatory examinations is minimized. The use of other drugs, such as paregoric, is eliminated. The dye is administered orally, in tablet form, usually in a set of six tablets, each containing 0.5 gm. of the dye, given five minutes apart, with water, the evening before the examination.

The dye is picked up from the blood by the liver and excreted into the bile. In an effort to approximate the percentage concentration of Priodax in the bile, we examined the latter at suitable intervals after the oral administration of the dye to patients whose gallbladders had been removed and in whom there were drainage tubes in the common ducts. We found an average concentration of about 0.2 per cent. It is important to emphasize that this figure is only a very doubtful approxima-

[1] This study was aided in part by a grant from the Schering Corporation, Bloomfield, N. J., manufacturers of Priodax (brand of iodoalphionic acid). Accepted for publication in August 1948.
[2] Acknowledgment is made to Mr. Oscar S. Swarth of the Schering Corporation, who diligently collaborated in the development of the scale.

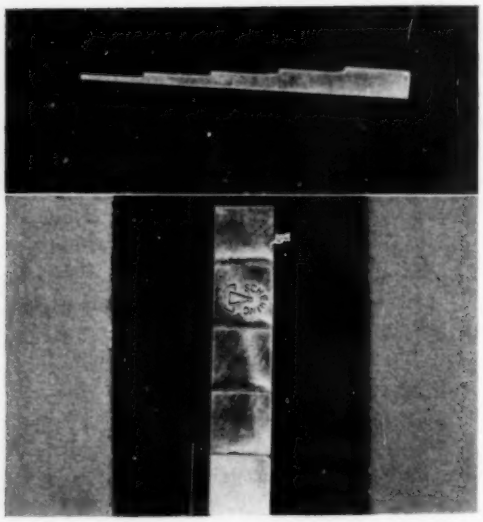

Fig. 1. Photographs of the scale.

tion, since the circumstances under which the tests were made were abnormal, and the exact percentage was very difficult to obtain.

The bile is conveyed in small amounts by the various-sized hepatic ducts into the main hepatic duct. The regulatory mechanism at the duodenal end of the common bile duct, consisting of the tonicity of the duodenal wall and the action of the sphincter of Oddi, during the fasting period, controls and diverts the passage of bile from the hepatic duct, through the cystic duct, into the gallbladder, where the dye is concentrated by loss of water and other substances through absorption and by the addition of mucin derived from the gallbladder mucosa. This absorptive power or concentration ability is one of the very important factors in visualizing the normal gallbladder after the administration of dye and in determining the density or the degree of opacification.

At the beginning, the possible range of concentration of the dye in gallbladders was unknown to us. We proceeded without any data from the literature. By trial and error we actually found that the dye is concentrated up to 4 or 5 per cent in the gallbladder. This was determined by comparing the density of the opacified gallbladder during cholecystography with the density of the standardized stepped scale, described more fully below. The first finished scale had only four steps (1 to 4 per cent), and although the few extreme densities actually encountered most nearly matched the 4 per cent step, there was occasionally a question as to whether the concentration was not somewhat greater. We considered and finally added the fifth step, or 5 per cent, first as a contrasting step to help us to decide on step 4 as against step 5 and, second, on the possibility that such a concentration might occur normally or pathologically (debatable), as in papillomatous disease of the gallbladder (2). The findings, therefore, suggest a concentration of 20 to 25 times. This concentration, however, may not actually be so large, owing to the doubtful character of the 0.2 per cent concentration of the dye in the bile coming from the liver.

The scale, as pictured (Fig. 1), consists of five steps made from aluminum bar stock. Step one, the thinnest, and therefore the most radiolucent, is 44/1,000 of an inch in thickness. The second step is a multiple of two, and so on, until the fifth or thickest step, which is 220/1,000 of an inch or five times the thickness of step one. These five steps were determined and standardized experimentally by utilizing human and artificial gallbladders with walls of radiodensity equivalent to the normal. These organs were filled to a capacity of 40 c.c. and measured 7.5 to 9 cm. in length and 3 cm. in their greatest breadth. They were filled with different concentrations of Priodax and roentgenograms were obtained simultaneously on the same film with varying scale thicknesses, until a visual match was secured. The following equivalents were obtained (for a 40-c.c. capacity gallbladder):

Step 1, 44/1,000 in. thick, to 1% concentration.
Step 2, 88/1,000 in. thick, to 2% concentration.
Step 3, 132/1,000 in. thick, to 3% concentration.
Step 4, 176/1,000 in. thick, to 4% concentration.
Step 5, 220/1,000 in. thick, to 5% concentration.

Since there is a definite cycle for the

behavior of each individual cholecystographic medium, the periods for radiographic examination are predetermined. The interval after the oral administration of Priodax is usually sixteen hours.

The roentgen technic is very simple. After the patient is positioned and before the exposure is made, the scale is placed between the patient and the x-ray table laterally on the right side between the iliac crest and the last ribs, as indicated in Figure 2. The film is exposed and processed in the usual way. Thus the scale is subjected to the same possible technical variations as is the opacified gallbladder. The procedure is rapid and does not interfere with the diagnostic value of the film.

If the size of the gallbladder is within the usual normal range, the density is matched against one of the steps and the concentration read off directly from the step numbers. A slight variation in size will not significantly alter this reading. If, however, the size is abnormal, the concentration is easily obtained by dividing the matching step number by the relative size of the visualized gallbladder. For example, if the gallbladder matches step 2 in density and is twice the normal expected size, the concentration, obtained by dividing 2 by 2, is 1 per cent. If the gallbladder matches step 2 and is one-half the normal expected size, the concentration is obtained by dividing 2 by 1/2, namely 4 per cent.

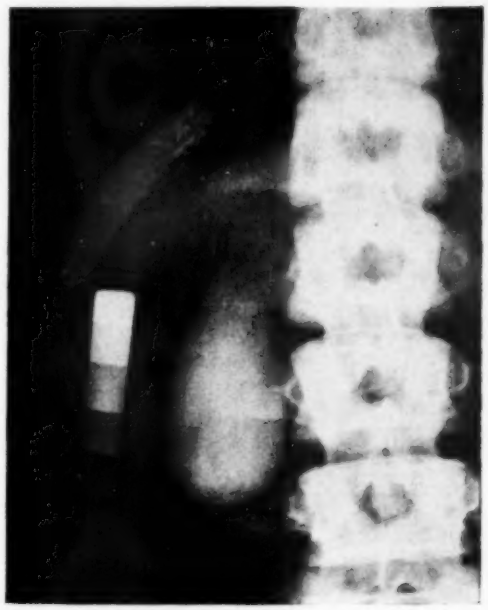

Fig. 2. Roentgenogram illustrating use of scale.

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SUMARIO

Técnica Rápida de Escala Cuantitativa para Calcular la Concentración Porcentaria de Priodax en la Vesícula Biliar durante la Colecistografía

Para medir la concentración de Priodax en la vesícula bilar durante la colecistografía los AA. emplean una escala de aluminio, que comprende cinco grados de espesor cada vez mayor, de 110/1000 a 550/1000 de 1 cm. Los cinco grados representan concentraciones de 1 a 5 por ciento.

En la práctica, se coloca la escala entre el enfermo y la mesa de rayos X de costado sobre el lado derecho entre la cresta ilíaca y las últimas costillas, exponiéndose después la película y trabajándose en la forma habitual. Si el tamaño de la vesícula biliar es normal o casi normal, puede determinarse el espesor directamente por la escala. Si el tamaño es anormal, se obtiene la concentración dividiendo el número del grado correspondiente por el tamaño relativo de la vesícula. Por ejemplo, si la vesícula alcanza el doble del tamaño normal y empareja el grado 2 en espesor, la concentración porcentaria es 2/2, ó 1 por ciento.

The Sensitometry of Roentgenographic Films and Screens[1]

RUSSELL H. MORGAN, M.D.,[2] and WILLARD W. VAN ALLEN, B. Sc.[3]

DURING THE PAST year, the Tuberculosis Control Division of the United States Public Health Service has established within its roentgenological facilities at Rockville, Maryland, a sensitometry laboratory for the testing of roentgenographic films, screens, and developing materials. The primary purpose of this laboratory is the procurement of reliable speed data on these products for the guidance of the Division in choosing the most satisfactory roentgenographic materials for its use. It is planned, however, to publish many of the data obtained from time to time and it is hoped, therefore, that this new facility will prove useful, also, to roentgenologists in general.

Although quantitative data giving the speeds of commercial roentgenographic films, intensifying screens, and developers will be of rather limited benefit at first, it is anticipated that the availability of such information will constantly stimulate the roentgen industry to improve the quality of its products. Also, it is expected that the experimental investigations conducted by the laboratory in the performance of its testing will yield much information which will be useful to roentgenologists in the improvement of their technical procedures. Furthermore, when automatic photoelectric timers become more widely used, the film-screen data will greatly facilitate the use of these instruments by making it possible to complete their adjustment simply by turning their sensitivity controls to the speed numbers of the films or film-screen combinations which are being used.

The institution of a program of roentgenographic sensitometry has required that a standard definition of film, screen, and developer speed be established and that methods of film, screen, and developer speed measurements be developed which comply with the definition. In the following paragraphs, the standard speed definition which has been adopted by our laboratory will be discussed in detail. Thereafter attention will be directed to a description of the equipment with which roentgenographic sensitometry is performed in compliance with this definition.

STANDARD DEFINITION OF ROENTGENOGRAPHIC FILM, SCREEN, AND DEVELOPER SPEED

Basic Considerations: In photographic practice, film speed is customarily defined as the reciprocal of the exposure required to produce a particular photographic effect;[4] that is,

$$S = \frac{k}{E} \qquad (1)$$

where S is the film speed, E is the exposure required to produce a particular photographic effect, and k is a constant of such magnitude that the values of S fall within a convenient range of numbers.

There can be little question that this definition is basically sound, since it assigns speed numbers to films in inverse proportion to the quantity of radiation required to affect them; that is, films which are darkened by a small amount of light will have higher speed ratings than those which require large amounts of radiant energy. Unfortunately, the particular photographic effect referred to in this definition has never been standardized by the photographic industry and, accordingly, a film may have a number of speed

[1] Accepted for publication in July 1948.
[2] Consultant, Tuberculosis Control Division, U. S. Public Health Service.
[3] Physicist, Tuberculosis Control Division, U. S. Public Health Service.
[4] For a complete discussion of the definition and measurement of photographic film speeds, the reader is referred to Mees (1).

ratings depending on the number of laboratories that have tested and published quantitative data upon it. In this country, the ratings determined by the laboratories of the Weston and General Electric Companies are among the most widely used.

At the present time, the particular photographic effect referred to in the speed definition is usually specified in either of two general ways. In one, a definite photographic density is indicated; for example, in the German DIN system (2, 3), the speed of a film is evaluated from the exposure required to produce a density of 0.1 above fog. Since photographic densities can be measured precisely, speed ratings derived from such a specification should be generally reliable. The density of a film is markedly affected, however, by the developing conditions employed in processing the film unless a developing time considerably in excess of normal is used. Accordingly, developing conditions must be meticulously controlled when this specification is employed.

The other specification of photographic effect is more complex and requires determination of the inertia exposure of the film under test. This exposure is derived by giving the film a series of graded exposures and plotting the resulting photographic densities against the logarithm of the exposure. A curve similar to that shown in Figure 1 will be produced. The linear portion of the curve is then extended downward until it crosses the log exposure axis. The point of crossing is the inertia exposure and is the value used in equation (1) to determine the film's speed. This specification has the advantage that in some films the inertia exposure is relatively unaffected by developing conditions and it is not necessary, therefore, to control development as precisely as when the density specification is used. However, the inertia exposures of many of the more highly sensitive films of recent years exhibit considerable instability with changes in development and the advantage of the specification is therefore questionable.

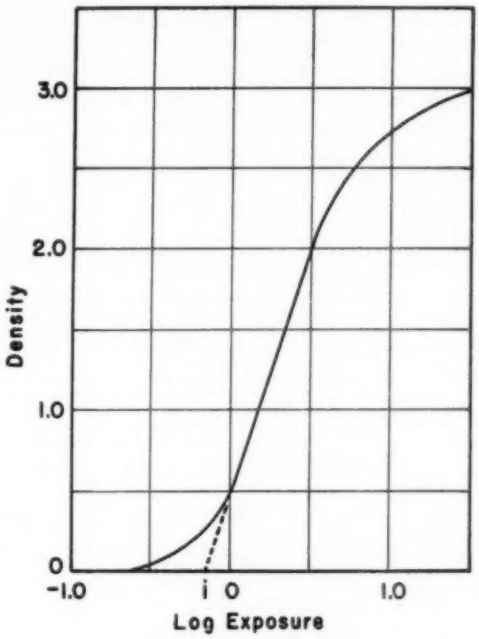

Fig. 1. Relationship between the logarithm of the exposure received by a typical photographic film and the resultant density of the film.

The speed of a roentgenographic film, like that of a photographic material, may be defined as the reciprocal of the exposure required to produce a particular roentgenographic effect. Such a definition immediately raises the question as to how the term, *particular roentgenographic effect*, should be specified. For a number of reasons, we favor a density specification. First, the density of a roentgenographic film is one of the most important factors controlling its interpretability (4). Such a specification, therefore, should yield roentgenographic speed numbers of practical significance to the roentgenologist. Furthermore, roentgenographic films customarily are developed to a point where the density is influenced only moderately by developing conditions, and it is anticipated that with wider use of automatic timing methods, long development times, in which density is essentially unaffected by developing conditions, will be generally employed. Finally, the linear portions of the density-log exposure curves of roent-

genographic films are extremely short, thereby making the evaluation of their inertia exposures very difficult. It therefore seems that a density specification has much to recommend it. There remains only to decide what density shall be stipulated.

It has been previously suggested by one of us (4) that this density be of the order of 1.0. Such a density is midway in the useful range of film blackening and accordingly represents the average density of the significant portions of a correctly exposed roentgenogram. *It therefore seems reasonable to propose that the speed of a roentgenographic film be defined as the reciprocal of the exposure required to produce a film density of 1.0 above fog density and the density of the film base.*

The foregoing definition of roentgenographic film speed applies equally well whether a film is exposed with or without intensifying screens. The speed ratings of films exposed with screens will, of course, be considerably greater than those exposed to roentgen rays directly. Furthermore, the speed ratings of films exposed with screens will depend on the brand of screen employed. In view of the latter fact, roentgenographic films may have a number of speed ratings depending on the number of brands of intensifying screen that are available. To avoid confusion when speaking of the speed numbers of films exposed with screens, it is recommended that one refer to such numbers as representing the speeds of film-screen combinations rather than of films alone.

It has been suggested by a number of workers that separate sets of speed numbers be assigned to roentgenographic films and intensifying screens; the speed rating of any given film-screen combination could then be obtained merely by multiplying the speed of the film by the speed of the screen. It has been pointed out that by such a system, a film, when exposed with intensifying screens, would have only one speed rating and that, therefore, no opportunity to misinterpret speed data would occur. However, such a system has a number of serious disadvantages. First, a complete listing of the speed characteristics of available films and screens would require three sets of data—one set of speed ratings for films exposed with roentgen rays directly, one set of ratings for films exposed with intensifying screens, and finally one set of ratings for the screens themselves. The duplicity of ratings for films exposed with and without intensifying screens would almost certainly lead to confusion. Of course, this difficulty could be avoided if the same set of film speed ratings could be used regardless of whether the films were exposed with or without intensifying screens, but such a situation requires that the intensification factors of the screens be constant and completely independent of such conditions as the type of film and the quality of the exposing radiation. Since this is not so (5), two sets of film speed ratings are imperative. A second disadvantage is the confusion which would occur if one or more new types of intensifying screen were developed. At the present time, calcium tungstate screens are used exclusively by the profession. However, if screens having spectral characteristics somewhat different than those of calcium tungstate were developed (*e.g.*, zinc sulfide), then an additional set of ratings would be needed for the computation of the speeds of the new film-screen combinations.

From the foregoing, it is evident that separate sets of speed numbers for roentgenographic films and intensifying screens should be avoided. Instead, when a film is exposed with intensifying screens, the film-screen combination should be regarded as a unit with a single speed number assigned to it.

Specification of Unit of Exposure: The basic definition of roentgenographic film speed, presented in the preceding section, has little practical usefulness until the unit in which the roentgenographic exposures shall be measured is specified. One unit that will immediately suggest itself is the roentgen. However, such a fundamental unit as the erg/sq. cm. might also be considered. In addition, an arbitrary unit,

based on the use of such measuring devices as the photoelectric intensitometer, might prove useful.

As far as the erg/sq. cm. is concerned, this unit is of such small magnitude that it would be rather impractical in general use. Also, a unit based on intensitometric data would have little usefulness, since measurements made with photoelectric intensitometers are extremely difficult to standardize. Accordingly, the roentgen

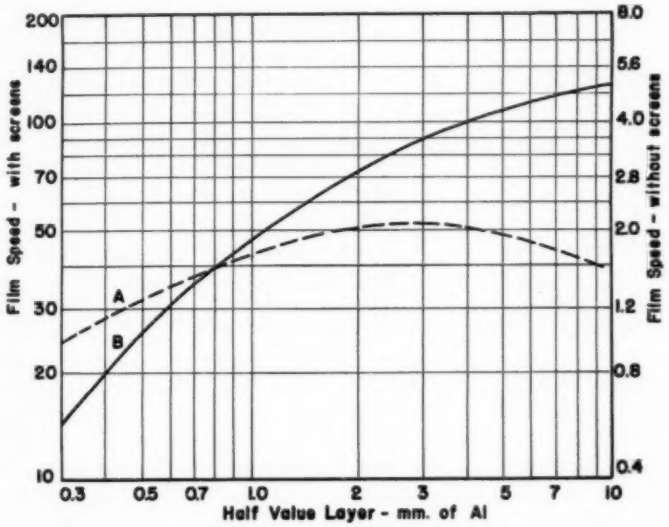

Fig. 2.—Speed of a typical roentgenographic film exposed to roentgen radiation directly (A) and of a typical film-screen combination (B) plotted as a function of the quality of the exposing radiation.

remains as the most suitable choice. Actually, it has much to recommend it. Its definition is well standardized and roentgenometric equipment through the years has been developed to a high degree of perfection.

The exposure required to produce a density of 1.0 in present-day roentgenographic films is of the order of 0.001 r when exposures are made with intensifying screens and 0.1 r when exposures are made with roentgen rays directly. Therefore, if the speed of a roentgenographic film were defined simply as the reciprocal of the exposure, measured in roentgens, required to produce a film density of 1.0, the speed numbers of present-day film-screen combinations and films exposed without screens would be in the neighborhood of 1,000 and 10, respectively. Such numbers seem inconveniently large and are likely to give a false impression of accuracy. Therefore it has been decided to adopt the deciroentgen (0.1 r) as the unit of exposure in this laboratory's speed definition. Such a unit will yield speed numbers in the neighborhood of 100 for film-screen combinations and 1 for films exposed without screens.

Specification of Roentgen Quality of Exposing Radiation: The use of the deciroentgen as the unit in which exposures shall be measured immediately requires that the quality of the exposing radiation be specified, for the speed of a roentgenographic film or film-screen combination, determined by roentgenometric testing, is markedly influenced by roentgen quality. This is well shown in Figure 2 where the speeds of a typical roentgenographic film, exposed to roentgen radiation directly, A, and of a typical film-screen combination, B, are plotted as a function of the quality of the exposing radiation (half-value layer of aluminum). These data were derived from sensitometric measure-

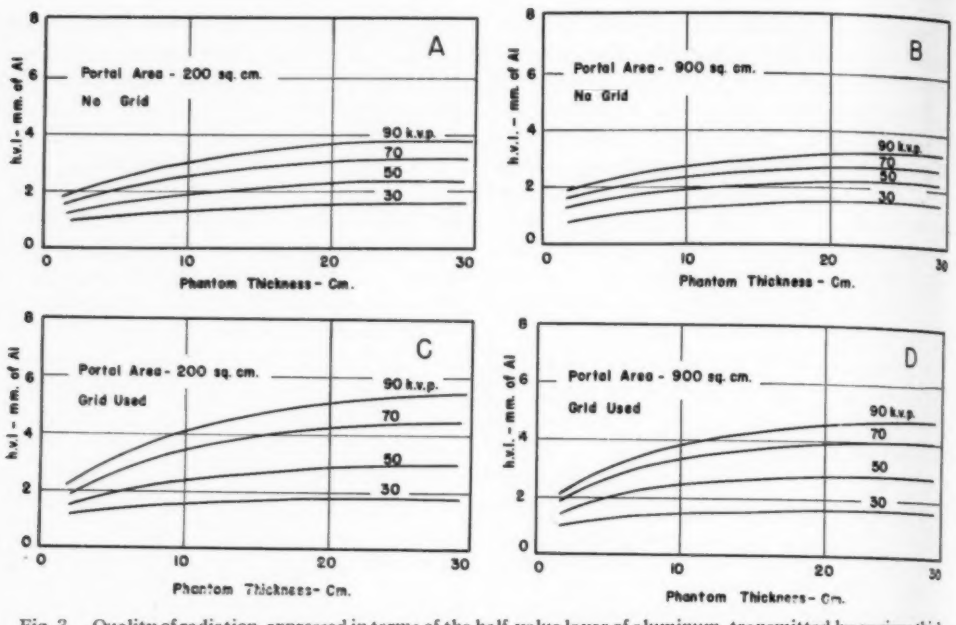

Fig. 3. Quality of radiation, expressed in terms of the half-value layer of aluminum, transmitted by various thicknesses of masonite presdwood (density = 1.07), for roentgen tube potentials ranging from 30 to 90 kv.p. for portal areas of 200 and 900 sq. cm. and for conditions under which a grid of 8:1 ratio is and is not employed below the phantom.

ments in which the exposures were recorded in deciroentgens.

In an effort to determine what quality of radiation should be specified in the speed definition, the authors measured the half-value layer in aluminum of radiation transmitted by phantoms of masonite presdwood (density = 1.07) ranging in thickness from 0 cm. to 30 cm. The incident roentgen radiation was produced by a four-valve, single-phase roentgen generator operating at 30, 50, 70, and 90 kv. (peak). The filtration in the roentgen beam included only the wall of the roentgen tube, which had an aluminum equivalence of 0.7 mm. The portal areas of the incident radiation were 200 and 900 sq. cm. Measurements were made with and without a grid, having a depth-space ratio of 8:1 and an element distribution of 50 lines per inch. Thus, the measurements were made through a range of conditions approaching those encountered in medical roentgenography.

The data derived from this investigation are plotted graphically in Figure 3. It will be observed that for conditions approaching those under which roentgenography is performed without intensifying screens (phantoms less than 10 cm. in thickness, kilovoltages less than 70 kv.p., and small portal areas), the half-value layer of the radiation ranged from 1.0 mm. to slightly over 3.0 mm. of Al; the average was approximately 2.0 mm. of Al. For conditions approaching those under which roentgenography is performed with intensifying screens (phantoms more than 10 cm. in thickness and kilovoltages over 50 kv.p.), the half-value layer of the radiation ranged from 2.0 mm. to almost 6.0 mm. of Al; the average was approximately 4.0 mm. of Al. Thus, it appears that when films are exposed without screens, a half-value layer of 2.0 mm. of Al should be specified as the quality of the exposing radiation; when films are exposed with screens, the specification should be a half-value layer of 4.0 mm. of Al. However, it will be noted from Figure 2 that the speed rating of the film exposed to roentgen radiation directly is essentially the same at a

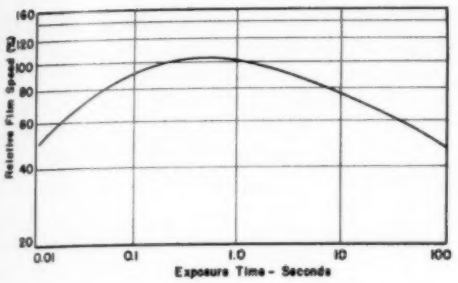

Fig. 4. Effect of exposure time on the speed of a roentgenographic film-screen combination.

half-value layer of 4.0 mm. of Al as it is at 2.0 mm. of Al. This is generally characteristic of all films exposed without screens (5). Accordingly, in order to simplify the specification of radiation quality in the speed definition, a half-value layer of 4.0 mm. Al has been adopted as the quality of the exposing radiation for both film-screen combinations and for films exposed with roentgen rays directly.

Specification of Radiation Intensity and Exposure Time: In practice, the speed of a roentgenographic film may be determined by giving the film a series of graded exposures of known roentgenage, measuring the resulting film densities and plotting a density *vs.* exposure curve. From this curve the exposure required to produce a film density of 1.0 can be readily evaluated and the speed of the film thereby determined from the speed definition.

Now the exposure received by a film is equal to the product of the intensity of the exposing radiation and the exposure time. Therefore, when the film is given its series of graded exposures, exposure can be varied by changing either the intensity of the radiation or the exposure time. However, the speed number of a roentgenographic film-screen combination when determined under one condition will not be identical to that determined under the other, due to the phenomenon of reciprocity law failure (6). Therefore, the method by which the exposure is controlled must be specified in the speed definition.

Under normal roentgenographic conditions, the intensity of the exposing radiation varies from point to point throughout the film, depending on the structure under examination, whereas the exposure time remains the same at all points on the film. Accordingly, it seems reasonable that, in the determination of the speed number of a film or film-screen combination, exposure be varied by changing the intensity of the exposing radiation and that the exposure time remain fixed.

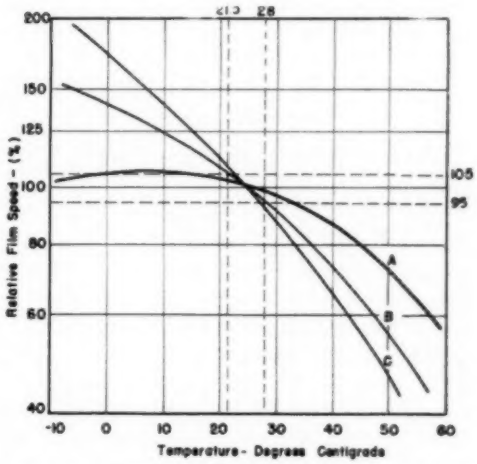

Fig. 5. Effect of ambient temperature on the speed of a typical roentgenographic film-screen combination. Curve A, exposure time of 0.1 second. Curve B, exposure time of 1.0 second. Curve C, exposure time of 10 seconds.

Because of reciprocity law failure, roentgenographic film-screen speeds are governed by the length of the exposure time. This is graphically illustrated in Figure 4, in which the speed of a typical film-screen combination is plotted as a function of exposure time. Exposure time, therefore, should not only be fixed at a given level during the measurement of the speed of a particular film but it should be fixed at a specific value for all film speed measurements.

At the present time, the exposure times used in normal roentgenographic practice usually approximate 1.0 second. It therefore appears that the speeds of film-screen combinations should be measured under conditions where the exposure time is 1.0 second. In the future, if high-powered

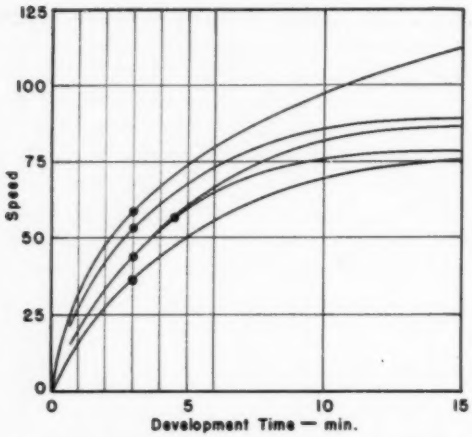

Fig. 6. Relationship between the speed and development time of a typical film-screen combination when processed in five different developers. The recommended development time for each developer is indicated on the corresponding curve by a circle.

roentgenographic equipment becomes more generally used, it may be necessary to lower the specification to 0.1 second.

Since films exposed to roentgen radiation directly do not exhibit reciprocity law failure, no specification of exposure time is required when referring to these films.

Specification of Temperature of Film or Film-Screen Combination at Exposure: It has previously been shown (7) that the temperature at which roentgenographic exposures are made has a considerable influence on the speeds of roentgenographic film-screen combinations. This effect is illustrated in Figure 5. It is evident that if speed measurements are to be reproducible, the temperature conditions within the exposing room must be well controlled. Since the temperature of an average roentgenographic exposing room approximates 25° C., such a temperature has been specified in the speed definition.

Specification of Developer Composition: Until now, attention has been focused principally on the conditions which should prevail during the exposure of a roentgenographic film or film-screen combination. However, the density produced in a film is strongly influenced also by the conditions which exist during its processing, and it therefore is of utmost importance that all factors dealing with the development process be rigidly specified in the speed definition. In Figure 6 the relationship between the speed of a typical film-screen combination and the time of development is shown for several commonly used developers. On each curve a point has been marked at the time of development recommended by the manufacturer of the developer. It is readily apparent that the speed of a film-screen combination depends on the developer employed. Not only is its speed different from one developer to another for the recommended development time, but the maximum speed obtained after prolonged development differs from one processing material to another.

In the establishment of a specification for developer composition, three possible choices present themselves: (1) a standard developer of ideal characteristics and special composition may be specified; (2) some one commercial developer may be chosen as standard; (3) the specification may call for no standard developer but instead may require that determinations of film or film-screen speed be made for each commercial developer. The first choice has little to recommend it. Such a developer would be difficult to obtain, since it must be compounded from separate ingredients and would not necessarily represent the behavior of *any* commonly used developer. Furthermore, if the speed numbers obtained by its use are to be of practical value, factors would have to be obtained to convert the speed of the film in the standard developer to the speeds of the film in commercial developers, a different factor being required for each developer.

The choice of a particular commercial developer as a standard has the advantage that the first two objections cited above for the special developer do not apply. However, the third objection does apply, and accordingly this choice leaves much to be desired. Since different developers produce different speeds regardless of development conditions, and since speed numbers to be useful must apply to

practical conditions of use, it has been decided that no fixed developer composition be specified in the speed definition but instead that speed numbers be determined for each developer with which a film or film-screen combination is used. Such numbers will therefore represent the speeds of film-developer or film-screen-developer combinations rather than those of films or film-screen combinations alone. This system of designation is entirely reasonable, since it is the combined action of film, screen, and developer that determines the over-all speed of the roentgenographic process.

Specification of Development Time: It has been pointed out in the preceding section that the speed of a film-developer or film-screen-developer combination is critically dependent on developing time. Therefore some specification of developing time must be included in the speed definition. It will be seen in Figure 6 that prolonged development yields speed values which are minimally affected by development time and which, therefore, are likely to be reproducible with greatest consistency. Such development, however, has the disadvantage that it does not follow conventional roentgenographic practice; furthermore, the high fog levels occasionally encountered after long development introduce problems which are not easily resolved and, finally, it is common practice to develop roentgenograms to a point on the steep portion of the density *vs.* development time curve in order to exercise some control over the density and fog of a roentgenogram. It seems reasonable, therefore, to specify that development shall be for the normal time recommended by the manufacturer of the developer used.

Specification of Developer Temperature: It is well known that the speed of a film-developer or film-screen-developer combination is influenced by the temperature of the developer. This is shown in Figure 7, in which the relationship between the speed and development time of a typical film-screen-developer combination is illustrated graphically for three different

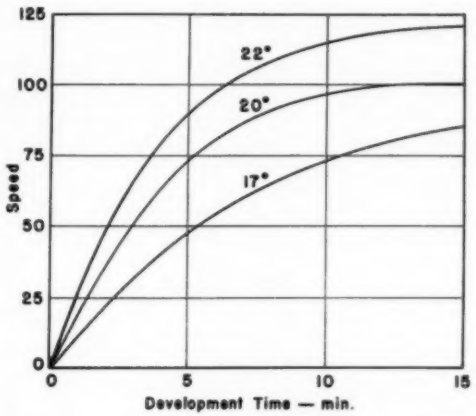

Fig. 7. Effect of developer temperature on the speed of a typical film-screen-developer combination.

temperatures. Since 20° C. is widely recommended and generally used as a developer temperature, this temperature has been specified in the speed definition.

Specification of Agitation During Development: The rate at which development proceeds within a roentgenographic film is governed in part by the rate at which the end-products of development are removed from the vicinity of the film. One may therefore expect that the speed of a roentgenographic material will be affected by the amount of circulation which the developer exhibits during the period of processing. Under conventional roentgenographic conditions, the only circulation that occurs within the developer is that resulting from convection flow. As such circulation is likely to be extremely erratic, the resulting data, if sensitometry is performed under these conditions, will not be consistently reproducible. For this reason, it is necessary to introduce methods by which the developer may be caused to flow regularly over the film surface.

In photographic sensitometric laboratories (1), developer circulation is usually provided by mechanical agitators consisting of paddles one or more inches in width and extending the length of the test film. The paddle surfaces are placed at approximately 80° to the surface of the film and travel in a direction parallel to

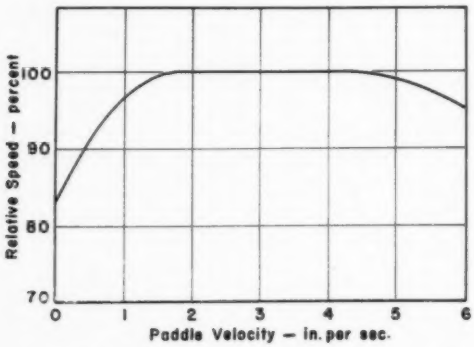

Fig. 8. Effect of agitation during development on the speed of a typical film-screen combination.

the film surface at a velocity sufficient to remove the end-products of development from the vicinity of the test film. This velocity is determined by measuring the speed of several samples of a test photosensitive material under conditions in which paddle speed is varied through a wide range. The velocity of motion at which the maximum speed of the material is obtained is taken as the optimum paddle velocity; it usually is in the neighborhood of 3.5 inches per second.

The foregoing system of agitation is also applicable to roentgenographic sensitometry. In Figure 8, the speed of a typical film-screen-developer combination is shown as a function of paddle speed. It will be seen that, when no agitation is present, the speed of the film is relatively low. As paddle speed increases, however, the speed of the combination increases, reaches a maximum level which prevails over a relatively wide range, and then slowly diminishes at high paddle velocities. The drop in speed at high velocities apparently is caused by the formation of eddy currents in the developer which prevent the removal of used developer from the film surface. From Figure 8 it seems adequate to require that roentgenographic sensitometry be performed under conditions in which the developer is mechanically agitated by paddles moving at an average rate of 2 to 4 inches per second.

Specification of Drying Conditions: Some evidence (8) has been presented in the literature which indicates that the density of a photosensitive material is affected by the rate at which the material dries after processing. In an effort to determine the effect of drying conditions on the speeds of roentgenographic materials, speed measurements were made on several typical film-screen-developer combinations with the films (*a*) dried in a cabinet without ventilation and without heating of the air, (*b*) dried in the open air, (*c*) dried in a cabinet with forced ventilation and without heating, and (*d*) dried in a cabinet with forced ventilation and with heating of the air. These various conditions yielded widely different drying rates in the films.

The results of these tests indicate that, under the conditions studied, no significant variation occurred in the speeds of the several materials. It has therefore been decided, for the time being at least, that no specification will be adopted in the speed definition for the drying conditions of films following processing.

Recapitulation: From the evidence presented in the foregoing sections the speed of a roentgenographic film-developer or film-screen-developer combination has been defined for sensitometric testing in this laboratory as the reciprocal of the exposure, measured in deciroentgens, required to produce a film density of 1.0 above base and fog under the following exposing and processing conditions:

1. The exposure time of the film or film-screen combination shall be 1.0 second.
2. The exposing radiation shall have a quality such that its half-value layer is 4.0 mm. of Al.
3. The ambient temperature of the film and screen during exposure shall be 25° C.
4. The temperature of the developer during processing of the film shall be 20° C.
5. The time of film development shall be that recommended by the manufacturer of the developer.
6. Continuous agitation of developer, equivalent to that created by paddles moving at an average speed of 2 to 4 inches per second, shall be provided during processing of the film.

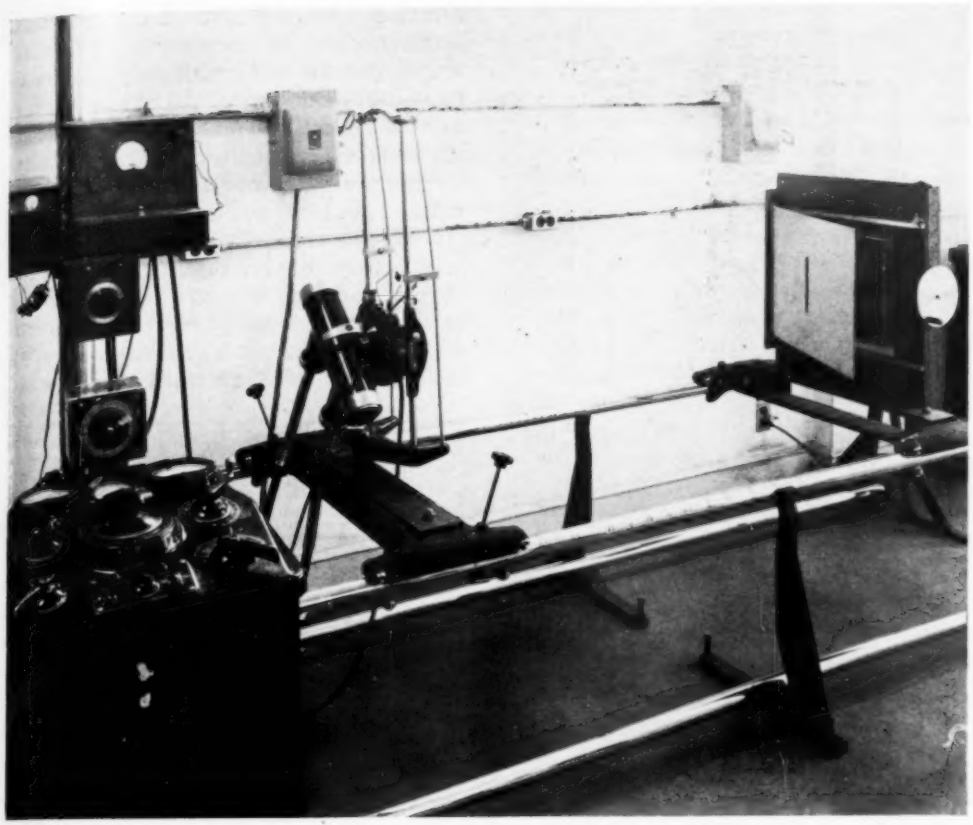

Fig. 9. Apparatus for giving graded exposures of measured roentgenage to test films and film-screen combinations.

This definition is likely to yield speed data that are consistently reproducible under conditions that approach as closely as possible those occurring in normal roentgenographic practice. In a few instances, the specifications of the definition deviate somewhat from conventional procedure. However, these deviations exist only in so far as it is necessary to guarantee reproducibility of results. Doubtless the specifications will require alteration from time to time as changes in roentgenographic procedure occur. These alterations will be made as promptly as warranted.

METHODS OF MEASURING THE SPEEDS OF FILM-DEVELOPER AND FILM-SCREEN-DEVELOPER COMBINATIONS

The roentgen sensitometric laboratory that has been established at Rockville comprises a pair of specially designed exposing and processing rooms by which roentgenographic speed measurements may be made in compliance with the speed definition discussed in the preceding sections. The exposing room is maintained at a constant temperature of 25° C. The nucleus of the exposing equipment included in the room is a horizontal optical bench (Fig. 9) by which graded roentgen exposures may be given to films or film-screen combinations under test. The bench consists of a pair of sturdily anchored tubular rails on which are mounted a film carriage, readily movable from one end of the bench to the other, and a roentgen tube, fixed in position at one end of the device. By varying the distance between the roentgen tube and the film carriage, the intensity of the radiation exposing the films or film-

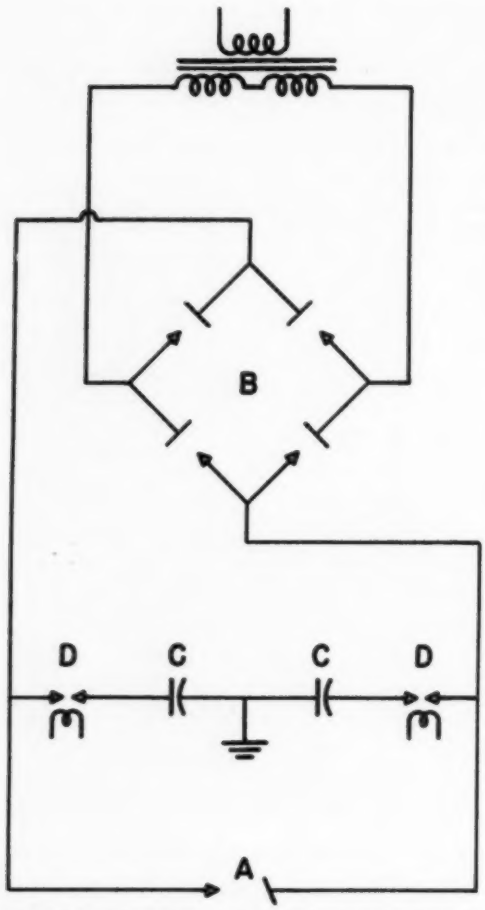

Fig. 10. Connection of capacitance to four-valve generator for constant potential output. A. X-ray tube. B. Valve tube network. C. Capacitors. D. High-tension switches.

screen combinations may be altered at will.

The film carriage includes an 8 × 10-inch cassette holder and is covered by a lead protective shield in which a slot, 8 inches long and 1/2 inch wide, has been cut. Also included in the carriage is a mechanism by which the cassette holder may be moved laterally behind the slot in order that different portions of the test film may be uncovered during successive exposures.

The roentgen tube, a Machlett Aeromax 15, is powered by a constant potential generator consisting of a conventional four-valve, single-phase generator with the addition of two 0.015 mfd. condensers connected in series across its output terminals. A generator of the constant potential type was chosen for this installation in order to maintain the quality of the exposing radiation as constant as possible. The generator includes a synchronous timer adjusted to produce exposures 1.0 second in duration. Also included in the generator circuit are two high-tension switches (Fig. 10) arranged to connect the condensers in the circuit when the exposure is initiated and to disconnect them when the exposure is terminated. These switches prevent a charging surge at the start of each exposure

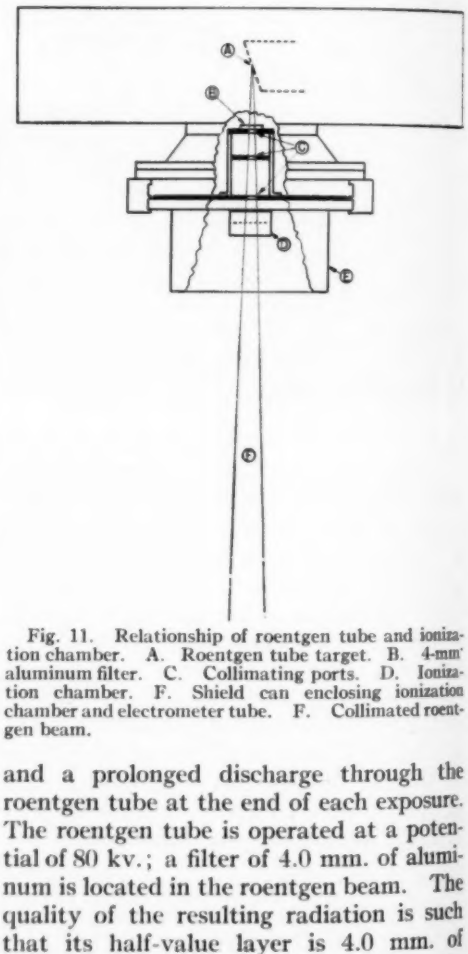

Fig. 11. Relationship of roentgen tube and ionization chamber. A. Roentgen tube target. B. 4-mm aluminum filter. C. Collimating ports. D. Ionization chamber. F. Shield can enclosing ionization chamber and electrometer tube. F. Collimated roentgen beam.

and a prolonged discharge through the roentgen tube at the end of each exposure. The roentgen tube is operated at a potential of 80 kv.; a filter of 4.0 mm. of aluminum is located in the roentgen beam. The quality of the resulting radiation is such that its half-value layer is 4.0 mm. of aluminum, the quality required by the speed definition.

The number of deciroentgens received by the film during each exposure is measured by means of an ionization chamber placed in the roentgen beam in such a way that all radiation striking the film passes through the chamber (Fig. 11). An integrating electrometer circuit in conjunction with this chamber (Fig. 12) serves to measure each exposure as it is made.

The ionization chamber is of the parallel-plate, open-air type and is made of rolled beryllium 0.2 mm. thick to reduce absorption to a minimum. The chamber, collimating diaphragms, and portions of the electrometer circuit are mounted as a unit adjacent to the roentgen tube. The chamber, however, is located sufficiently far from the aluminum filter to prevent a significant quantity of scattered radiation, arising in the filter, from reaching the chamber. The system has been calibrated against the standard chamber of the National Bureau of Standards.

The darkroom of the laboratory includes a stainless steel processing unit consisting of water-jacketed developer and fixing tanks and conventional washing baths. The water in the jackets is continuously circulated and solenoid valves, controlled by a mercury thermostat, permit hot and cold water to enter the circuit alternately in order to maintain a constant developer temperature. The system provides a water-jacket temperature of 20° ± 0.1° C. and a developer temperature of 20° ± 0.02° C.

Agitation during development is accomplished by means of two stainless steel paddle assemblies inserted in the developer tank and arranged to move horizontally across the film, 1/4 inch from the film surface in a simple harmonic reciprocating motion. The paddles are driven by an electric motor through suitable speed-reducing gears to give a paddle speed of 50 oscillations per minute (an average velocity of 3.75 inches per second). The distance between blades and the length of the travel are so adjusted that there is approximately 50 per cent overtravel. Thorough agitation is thus assured without danger of a static area developing between paddles. Furthermore, each paddle is inclined to the film surface at an angle of about 80°. This serves to produce a mixing motion of the developer as well as to move it past the film surface. A schematic diagram of the paddle assembly is shown in Figure 13.

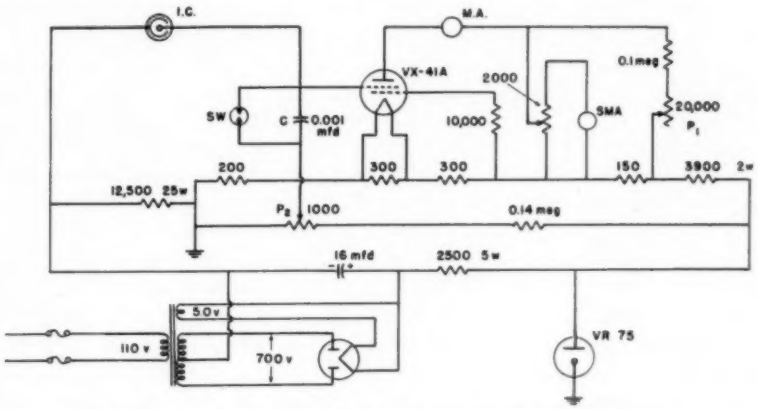

Fig. 12. Electrical circuit of integrating roentgen exposure meter.

Speed measurements are made with the foregoing equipment by placing the roentgenographic film or film-screen combination under test in the film carriage of the optical bench and giving it a series of graded exposures. The amount of each exposure given to the film is measured in deciroentgens by the ionization chamber system through the application of the

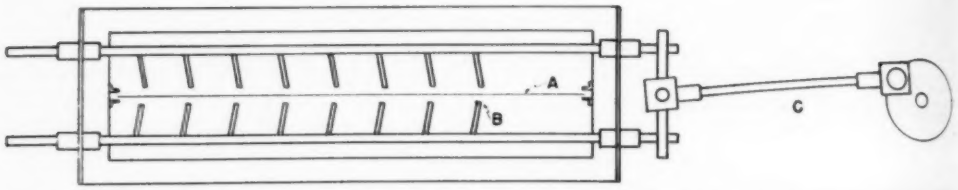

Fig. 13. Schematic diagram showing top view of developer agitation mechanism. A. Roentgenographic film. B. Paddles. C. Reciprocating drive mechanism.

inverse-square law relating roentgen intensity and tube-film distance. Corrections for air absorption of the roentgen beam are necessary for tube-film distances greater than 50 cm.

After exposure, the film is processed for a length of time recommended by the manufacturer of the developer and, when dry, is measured densitometrically. Corrections are then applied for fog density according to the Wilsey (9) formula, and the resulting densitometric data are plotted graphically as a function of the quantity of exposing radiation. Thereupon, a curve is drawn through the several points and the exposure in deciroentgens necessary to produce a film density of 1.0 is determined. The reciprocal of this exposure value is the speed of the film-developer or film-screen-developer combination.

At the present time, speed data on commercially available films, screens, and developers are being collected as rapidly as possible. As this material comes to hand it will be published in *Public Health Reports*. From time to time it is hoped that summary reports will also be published in the roentgenological journals.

SUMMARY

A roentgen sensitometric laboratory has been established by the U. S. Public Health Service to measure the speed characteristics of the commercially available films, screens, and developing materials used in medical roentgenography. The data are collected by determining under rigidly controlled conditions the exposures or quantities of roentgen radiation, measured in deciroentgens, necessary to produce film densities of 1.0 in the film-developer or film-screen-developer combinations under test. The speeds of various combinations are then calculated from the reciprocals of the exposure data.

As the laboratory proceeds with its program, information on the speed characteristics of many roentgenographic films, screens, and developers will be published regularly. It is hoped that such information will not only be of technical value to roentgenologists but will also constitute a constant stimulus to the roentgen industry to improve its products.

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SUMARIO

La Sensibilimetría de la Películas y las Pantallas Roentgenográficas

El Servicio de Sanidad Pública de los E. U. A. ha establecido un laboratorio roentgenosensibilimétrico para medir las características de velocidad de las películas, pantallas y sustancias reveladoras empleadas en la roentgenografía médica y puestas a la venta. Los datos se compilan determinando, en condiciones rígidamente comprobadas, las exposiciones o cantidades de irradiación roentgen, medidas en decirroentgens (0.1 r), que se necesitan para producir densidades de película de 1.0 en el revelador de películas o en las combinaciones de reveladores de películas-pantallas en vías de comprobación. Las condiciones estipuladas son: tiempo de exposición, 1.0 segundo; calidad de la irradiación de exposición tal que su capa de hemirreducción sea 4.0 mm. de aluminio; temperatura durante la exposición, 25° C.; temperatura del revelador, 20° C.; tiempo de revelado, el recomendado por el fabricante del revelador; agitación continua del revelador equivalente a la creada por paletas que se movieran a una velocidad media de 5 a 10 cm. por segundo. Las velocidades de varias combinaciones se calculan por las recíprocas de los datos de exposición.

A medida que el laboratorio prosiga con sus planes, publicará con regularidad datos relativos a las características de velocidad de muchos reveladores, películas y pantallas roentgenográficas esperando que esta información no sólo sea de valor técnico para los radiólogos sino que constituya un constante aliciente a la industria roentgenológica para mejorar sus productos.

Relationships Between Chemical and Biological Effects of Ionizing Radiations[1]

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IN RADIOBIOLOGY we are interested in chemical effects of ionizing radiations only in so far as they may be involved in biological effects.[2] As background for discussion of this relationship, let us briefly review the general state of our knowledge (or ignorance) of mechanisms of radiobiological actions:

1. The first event in such an action is, of course, the absorption of radiant energy by molecules in the biological object or its medium. The molecules which thus acquire energy in excess of normal are said to be activated. Some absorb so much energy that electrons are ejected; these molecules are said to be ionized. Others absorb less energy; electrons are merely shifted to other orbits; such molecules are said to be excited. The foregoing physical processes are at present fairly well understood, and many aspects of them can be described quantitatively.

2. After the absorption of energy, our knowledge of the radiobiological action is practically zero until the biological effect occurs. This effect—depending upon the biological object irradiated, the conditions of irradiation, the technic of observation, and a multitude of other factors—may be the mutation of a gene, the breaking of a chromosome, an increase in permeability of a membrane, an inhibition of cell division, a leukopenia, induction of a neoplasm, death of an animal, or any one of many other radiobiological phenomena. In all these diverse cases, however, there is no apparent resemblance between the biological effect and the initial physical phenomena associated with the absorption of energy.

3. From the foregoing considerations, it is evident that, during the so-called "latent period" which intervenes between the energy absorption and the observation of biological effect, a chain of important connecting events must occur. So far as I am aware, the specific nature of these events is in all cases unknown, as is also the number of successive events in the chain. However, *in general* it appears highly probable—and most physicists and radiobiologists have long considered it almost axiomatic—that at least the early events in the chain are chemical.

Indeed, it is exceedingly difficult to imagine a mechanism of radiobiological action which does not involve chemical changes. The biological end-effects are changes in either physiology or morphology, these terms being used in the broad sense. The physiological changes clearly are changes in cell chemistry or are the results thereof. Moreover, when we recall that biological structures are built by chemical means, we can hardly imagine a morphological change which does not involve chemical change. Let us also consider the early part of the mechanism of radiobiological action. The high-energy radiations can ionize any type of molecule, and we may be confident that many kinds of molecules in the cell are thus highly activated under irradiation. Once a pair of ions is formed, they may do one of two things: They may recombine, in which case no change is produced in the cell.

[1] Presented at the Thirty-fourth Annual Meeting of the Radiological Society of North America, San Francisco, Calif., Dec. 5–10, 1948.

[2] It might be helpful to comment on the terms "biological" and "chemical" as used here. Biological structures, of course, consist of chemical substances, and biological activities are made up of chemical and physical processes. When we know something of the molecules involved in the structures and processes, we usually speak of chemical composition and chemical reactions. When we are ignorant of the molecules involved, we fall back on the term "biological."

Or they may form new combinations, either with other radiation-produced ions or, more likely, with the much more numerous non-activated molecules in the cell. This production of new combinations is, by definition, chemical reaction. In other words, it would appear, from this type of reasoning, that chemical reaction is the only way in which the initial physical act of ionization may start any kind of change in the biological object.[3] This conclusion is substantiated by numerous experimental observations that various cellular constituents, ranging in complexity from molecular oxygen to the most complicated proteins, undergo chemical change when irradiated *in vitro* in aqueous solution.

Henceforth I shall assume that chemical effects do intervene between energy absorption and observation of the biological effect. There remain to be discussed (*a*) the nature of these chemical reactions and (*b*) the manner in which they lead to the biological effect.

How many kinds of chemical reaction are directly initiated by irradiation of a living cell? At first thought, the upper limit on the number of possible ones would appear to be enormous, because (*a*) the known kinds of molecules in a cell number at least in the hundreds, and the total is probably much greater; (*b*) the ionizing radiations are capable of activating any of these many molecular species; and (*c*) there is the possibility that any type of activated molecule may react with any type, activated or non-activated, in the cell.

Actually, the foregoing considerations lead to an exaggerated estimate of the number of kinds of reactions produced. In the first place, many kinds of molecules will not be affected. For instance, 1,000 roentgens of x-radiation ionize only about one molecule in ten million in a typical cell. Accordingly, those molecular species which occur only in small numbers per cell[4] stand a high probability of not being ionized and of not being close enough to an ionized molecule to react with it before it reacts with something else. In the second place, some of the possible new combinations of ionized molecules with other molecules are energetically impossible or highly improbable.

However, despite these factors tending to reduce the actual number of kinds of reaction, the figure still is probably quite high. This, occurring at the outset of the radiobiological action, makes the unraveling of the mechanism appear at first glance practically hopeless. The situation does not seem so bad, however, when one reflects that, after all, not all the types of reaction which occur are necessarily involved in any given biological effect. That this must indeed be true is supported by the following observations.

First, for several diverse biological effects (11, 19, 20, 23) it has been demonstrated that irradiation of the cell nucleus is far more effective than irradiation of cytoplasm. Accordingly, in such cases, we can locate the pertinent reactions, or at least the early ones, in a definite morphological fraction of the cell. Second, when different radiobiological effects are studied in the same species of cell, it is sometimes found that the quantitative relationships between dose and the various effects can be altered in different ways by the same agent. For instance, Gray and his coworkers (9, 10) studied the effectiveness of various radiations in lethal action and in inhibition of mitosis in the root of the broad bean. They found that for both effects the efficiencies of the radiations varied with their specific ionization,[5] but that the quantitative relations between efficiency and specific ionization were drastically different in the two cases. Another instance: Crabtree (3) used variations in temperature to alter the partial inhibition

[3] Similar reasoning can be applied to the excited (but not ionized) molecules. These may lose their activation energy by some process which restores the molecule to normal—*e.g.*, emission of low-energy radiation—or they may react with other molecules, *i.e.*, undergo chemical change.

[4] It is to be remembered that many molecular species of extreme importance (genes) occur only one or two per cell.

[5] This is discussed later in more detail.

by radiation of various metabolic processes in surviving tissues. All of the radiobiological effects varied quantitatively with temperature, but in widely different ways.

Experimental results like those just described are completely unexplainable on the assumption that all types of radiation-induced chemical reactions in the cell contribute significantly to each biological effect. On the other hand, they are completely consistent with the view that each biological effect is due to a limited number of specific types of reactions. Reaction types which play a role in a given biological effect are termed *relevant* to that effect. All others are *irrelevant* to it, although certain ones may be relevant to other effects in the same biological object.

When do the relevant reactions occur? The first ones must occur very soon after the ions are formed, because the average life of an ion is a millionth of a second or less. If reaction does not occur within that time, the ions recombine and no net change occurs. The later relevant reactions obviously take place during the remainder of the "latent period," which, depending upon the nature of the biological effect and the technic of observation, may last anywhere between a few minutes and a few decades.

It is of further interest to consider the location of the relevant reactions. It is plain that the very first ones must occur close to the locations of the ions immediately after their formation, because the short life of the ions permits them little time to diffuse or otherwise be moved away. From the ionization process we obtain a very light negative ion (the ejected electron) and a heavy positive ion (the residual molecule). Usually the energy absorbed is somewhat greater than that required to eject the electron, and the excess appears as kinetic energy of the two ions, their movement being in opposite directions. Because of its relatively great mass, the positive ion gets a very small fraction of this energy and stays practically at the point where ionization takes place (except for the influence of diffusion and convection, which must be small during the life of the ion). The negative ion (electron) accordingly gets practically all of the kinetic energy and, being light, it starts off with fair velocity and may go some little distance (on a molecular scale) before it is brought to thermal equilibrium by collisions with neighboring molecules. Thus the positive and negative ions are separated immediately after formation. Lea calculates that this separation is of the order of 15 millimicrons in the case of an alpha-particle track in water (16).

The foregoing spatial considerations are concerned with events on a molecular scale. Let us now consider the sites of reaction on a larger scale. If the first reactions occur near the points where ions are formed, then the sites of the individual early reactions must have substantially the same distribution as the ionizations. About this we have considerable information. Wilson cloud-chamber photographs, which record the location of ions in gases, show that the ion pairs are not produced singly at random in an irradiated volume but are distributed along the tracks of the speedy ionizing particles (electrons or atomic nuclei) which either constitute the primary radiation (*e.g.*, alpha or beta rays) or are secondary to other types (*e.g.*, x-, gamma, or fast-neutron rays). Moreover, these photographs reveal considerable information about the distribution of the ion pairs along the tracks. They are not always single but are frequently in clusters consisting of two or more pairs, the average number being three (13). The clusters, moreover, are not uniformly spaced along the tracks but are closer together the less the speed of the ionizing particle. This means that the ion pairs are, on the average, closer together near the end of the track than at the beginning.

The number of ions produced per unit length of track of ionizing particle is called the *specific ionization* or linear *ion density*. Not only does it vary along the track of an individual ionizing particle, but it is widely different at comparable positions along the tracks of different types of particles,

e.g., electrons and alpha particles. Although the Wilson photographs, it is true, reveal the foregoing facts about ionization tracks in gases only, additional physical data and theory make it relatively safe to assume that the picture in an irradiated cell is substantially the same, except reduced in dimensions about a factor of a thousand.

In view of the marked differences in distribution of the ion pairs, and accordingly of the early chemical reactions, along the ionization tracks, one might wonder whether this distribution might affect the efficiency of the radiation per ion pair, or, putting it otherwise, alter the biological effectiveness of the early relevant reactions. This is indeed the case. Over a hundred investigations are to be found in the literature, in each of which two or more radiations producing substantially different specific ionization were used in producing the same biological effect. In practically all of these experiments the various radiations were found to vary in biological effectiveness with their specific ionizations. (See reference 25 for review.)

Looking at the picture on a microscopic rather than submicroscopic scale, we may make a few more comments about the location of the early relevant reactions. It has already been mentioned that fractional irradiation of parts of cells has shown that, in production of several different biological effects, ions produced in the cell nucleus are much more effective than those produced elsewhere. In these cases, the early relevant reactions obviously take place in the nucleus, although in some cases the end-effects—*e.g.*, inhibition of chlorophyll formation (23)—are observed outside the nucleus.

Let us consider another example of locating the early relevant reactions. Various types of chromosome aberrations have been much studied and have been reviewed by Lea (15) and by Catcheside (2). All of them can be shown, by cytogenetic methods, to be due to breaks induced either in chromosomes or half-chromosomes (chromatids). Accordingly, the radiochemical reactions of interest are those relevant to breaks. The highly localized nature of the breaks strongly suggests that all the relevant reactions occur very close to the location of the break and, indeed, probably originate with ions produced along a track which passes through or very near the chromosome. However, this assumption, unsupported, turns out to be rather naïve when it is found that certain dissolved substances, such as nitrogen mustards, can also produce chromosome breaks. Since these chemicals certainly are not *applied* locally to portions of chromosomes—even though they might *concentrate* in such a fashion—it is plain that radiation might produce a substance extrachromosomally which nevertheless could produce the breaks.

To support the idea of early relevant reactions in or near the chromosome, more evidence is needed, and it is now available in apparently sufficient amount. Rather typical of this evidence is the following (2). To produce certain types of chromosome aberration (exchanges), it is necessary that both chromosomes be broken. When these aberrations are produced by fast neutrons, their number varies directly with dose, but when produced by x-rays the number varies with the square of the dose. Now, if the relevant reactions occur distant from the chromosomes, either of these two dose-effect relationships would be consistent if it held for *both* types of radiation, because the hypothetical substance producing the breaks would have to diffuse a considerable distance and accordingly there should be no appreciable effect of the submicroscopic differences in distribution of the ions and the early relevant reactions produced by the two types of radiation. However, since the dose-effect relations are not the same, the only way in which distant reactions can still be invoked is to postulate *different* relevant reactions, and this seems to be highly unlikely. In contrast to all these difficulties, it is easy to explain the observed dose-effect relations in terms of relevant reactions in the chromosomes. If one

assumes that the neutrons, known to produce a relatively short length of dense ionization tracks, break both chromosomes simultaneously, while the x-rays, known to produce a great length of sparse tracks, break only one chromosome at a time, the two types of dose-effect relation are mathematically predictable. Such an assumption, of course, implies highly localized relevant reactions. Since the assumption is logically tenable, the idea of localization of the reactions is supported.[6]

As a further example of locating the early relevant reactions, we may consider certain biological effects which are reduced in amount by adding certain organic substances to the medium of the cell for the duration of irradiation (5, 17). Since some of these substances (*e.g.*, proteins) almost certainly do not penetrate the cell membrane, it seems reasonable to conclude that, in the production of these biological effects, the early relevant reactions must occur in the medium rather than in the cell. Later relevant reactions must, of course, occur at the cell surface (or possibly even inside the cell after cellular absorption of products of the early relevant reactions).

Let us now consider the chemical nature of the relevant reactions. Here we must invoke our present knowledge of the chemical constitution of the cell, of the radiation chemistry of its constituents *in vitro*, and of the natures of the biological end-effects.

The end-effects observed are mostly deleterious and are usually qualitative abnormalities—such as chromosome aberrations or inhibition of cell division—although quantitative changes in normal cellular processes are also sometimes observed. There are two general means by which such changes might be accomplished: (*a*) the chemical *destruction* of an important molecular species, such as an enzyme, vitamin, or gene, and (*b*) the *production* of a molecular species which, in the broad sense, acts as a stimulus to the cell—for instance, a poison such as the much discussed hydrogen peroxide. In the latter case, the molecular species produced might be completely new to the cell or it might be normal to the cell but produced in excess. In any event, either a destruction or a production must be accomplished through chemical changes in molecules normally in the cell.

As pointed out earlier, any kind of molecule present in the irradiated cell may be ionized and accordingly stands a chance of being chemically altered. There is, however, one molecular species which is several times as abundant as all others taken together—the water molecule. Most of the molecules ionized are water molecules. Can a biological end-effect be due to a destruction of water molecules, thus depriving the cell of part of its water? This seems highly improbable. It has already been remarked that a reasonably large exposure (1,000 r) ionizes only about one molecule in ten million. If one ion pair should result in the destruction of one water molecule—and it appears unlikely that the yield of the reaction would be of a higher order of magnitude—the fraction of the water destroyed would be negligible from the standpoint of deprivation. Even if the yield were surprisingly high and a fairly large fraction of the water were thus removed from the cell, in most cases the cell would merely absorb water from its medium until the deficit was restored.

On the other hand, the ionized water molecules (or products of their reactions) might undergo relevant reactions with other cellular constituents. Indeed, in numerous investigations (*e.g.*, 8, 4, 7) it has been found that various cell constituents, ranging in complexity from molecular oxygen to enzymes, are altered if irradiated when dissolved in water, and

[6] It may be noted that chromosome breaks appear to be effects which can be handled by the target theory, one feature of which is the assumption that the pertinent radiobiological events are localized in small (usually submicroscopic) volumes in which "hits" must be produced. It is sometimes stated that the idea of relevant radiochemical reactions conflicts with target theory. However, there appears to be no conflict if one visualizes the relevant reactions occurring in highly localized fashion at various points along the ionization tracks. If enough relevant reactions occur close enough to an important small volume, they constitute a hit. Some biological effects may result from "hits," others from less localized relevant reactions.

that the quantitative relationships are consistent with the idea that they are altered by reaction with products formed from water. The radiochemical yield is independent of concentration of solute: so long as the molecules of dissolved substance are few in number compared to those of the water, the concentration of solute can be changed within wide limits without changing the number of molecules undergoing chemical reaction per unit dose. This is called the "dilution effect." It is, of course, unexplainable on the assumption that the solute molecules react as a result of their own ionization, for in such case the number of molecules changed per unit dose should be strongly dependent upon solute concentration, rather than independent, as observed. On the other hand, it is completely consistent with the view that the solute molecules react with ionized water molecules or reaction products resulting from them.

Substantiation of this latter view is furnished by the so-called "protection effect." When to a solution containing a single solute a second solute is added (*e.g.*, 4, 7), it is frequently observed that the number of molecules of the first solute changed per unit dose is reduced, and that the extent of this "protection" depends upon the relative concentrations of the two solutes. This is, of course, exactly what would be expected if the two solutes were both capable of reacting with the same product (or products) of water ionization and were competing for it. It is interesting to note a biological parallel, namely, that, in studying inhibition of fertilizing ability of sea-urchin sperm, Drs. Evans and Failla and their co-workers (5) have observed both the dilution effect and the protection effect.

I do not mean to imply in the last few paragraphs that all radiochemical reactions in cells must be initiated by ionization of water and are therefore of an indirect type. Direct reactions, due to ionization of the solute, must occur, although the yields are likely to be small compared to the indirect effects. Indeed, such solutes as enzymes can be chemically changed by irradiation in the dry condition, but the doses required to change a given percentage are usually greater by a factor of some hundreds or thousands than the ones equally effective on the same substance in dilute aqueous solution. Again it is interesting to note a biological parallel: Structures such as spores and seeds are much more resistant when dry than when moistened (12, 14).

Whatever may be the ultimate answer to the question of relative radiobiological importance of direct and indirect reactions, there is no doubt that at present most radiobiologists find the indirect reactions the more exciting, not only because of the reasons given above but also because their postulation appears the more fruitful in terms of new experiments suggested and designed. A great stimulus has been given this field by the recent theory of Weiss (21), according to which the ionization of water results in the formation of free hydroxyl radicals and hydrogen atoms which then undergo reactions with cell constituents, at least some of which are relevant to the end-effect. The main events, according to Weiss, are as follows: The passage of an ionizing particle ionizes water:

$$H_2O \xrightarrow{\text{radiation}} H_2O^+ + e^-. \qquad (1)$$

The positive water ion dissociates,

$$H_2O^+ \rightarrow H^+ + OH, \qquad (1.1)$$

forming a hydrogen ion and a hydroxyl radical. The electron becomes attached to a normal water molecule,

$$e^- + H_2O \rightarrow H_2O^-, \qquad (1.21)$$

and the resulting negative water ion dissociates to yield a hydroxyl ion and a free hydrogen atom:

$$H_2O^- \rightarrow OH^- + H. \qquad (1.22)$$

The electron may alternatively, but probably rarely, combine with a hydrogen ion to form a free hydrogen atom:

$$H^+ + e^- \rightarrow H. \qquad (1.3)$$

In addition to the foregoing reactions fol-

lowing the ionization of water, OH radicals may be formed by ejection of electrons from hydroxyl ions normally present in water:

$$OH^- \xrightarrow{\text{radiation}} OH + e^- \qquad (2)$$

The resulting electron may, of course, produce H atoms by reactions (1.22) and (1.3). Since OH^- ions are much less numerous than water molecules, reaction (2) probably occurs much less frequently than reaction (1).

After the hydroxyl radicals and the hydrogen atoms are formed, what can be predicted about their further history? If they are close enough together, they may recombine (21):

$$H + OH \rightarrow H_2O,$$

with the result that no net change occurs. However, as Lea has pointed out (16), the distance between H and OH is usually so large on a molecular scale that other things are likely to happen before diffusion brings them together. Some of the other things which may happen are as follows: If molecular oxygen is present (and it is in most cells), hydrogen peroxide may be formed by action of the free hydrogen atoms:

$$H + O_2 \rightarrow HO_2,$$
$$2HO_2 \rightarrow H_2O_2 + O_2.$$

Many investigators have observed H_2O_2 production in water containing oxygen, and the formation of this poison has often been invoked as a mechanism of radiobiological injury. Other reactions which may occur are oxidations such as ferrous to ferric ion,

$$Fe^{++} + OH \rightarrow Fe^{+++} + OH^-,$$

and iodide ion to iodine,

$$I^- + OH \rightarrow I + OH^-$$
$$2\,I \rightarrow I_2,$$

and reductions such as ceric to cerous ion,

$$Ce^{++++} + H \rightarrow Ce^{+++} + H^+.$$

These oxidoreduction reactions and many others have been observed to occur in irradiated aqueous solutions, and since it is well known that many important cell constituents, such as sulfhydryl-containing compounds, may be functionally changed by oxidation or reduction, it seems highly plausible that reactions of this type may be radiobiologically important.

Until a few years ago, there was a serious difficulty in accepting the reactions observed *in vitro* as relevant to biological effects. This was the fact that in general the doses required to produce biological effects were tens or hundreds of times smaller than those required to produce an amount of chemical change which plausibly might cause biological change. However, Dale (4) and others have recently shown that certain cell constituents (chiefly enzymes), when highly purified and irradiated in dilute aqueous solution with 100 r or less, are inactivated to an extent which conceivably might produce biological changes. There is still the objection that the irradiation *in vitro* does not accurately tell us what would happen quantitatively to the same substance when irradiated in a living cell, where all manner of protective (competing) substances might be present. However, the experiments prove that at least some important cell constituents are intrinsically radiosensitive enough that their radiochemical reactions in the cell might be relevant to biological effects.

Another glimpse of a possible explanation of radiosensitivity *in vivo* is furnished by the very recent work of Mazia (18), who finds not only that the enzyme pepsin is very radiosensitive when irradiated in a monomolecular film consisting of enzyme plus substrate (egg albumin), but that the sensitivity is markedly decreased by increases in surface pressure which may be expected to alter the structure of the film. This gives us a hint that morphology on the molecular scale may have much influence on radiosensitivity.

From the foregoing discussion we see that many radiochemical reactions of cell constituents are known to occur *in vitro* and that it appears reasonable that at least some of these known reactions, and probably many additional unknown ones,

occur in an irradiated cell. If we are interested in one certain biological effect, can we identify one or more of these many reactions as relevant to that effect? Such is our present state of ignorance that I must regretfully admit that I know of not a single case in which such relevance has been unequivocally established. And yet, obviously this is a step which we must learn to take in radiobiological research if we are to make substantial progress in understanding mechanism.

In view of the importance of the subject, it might be profitable to inquire: What is required to establish relevance? The minimal procedure would seem to be as follows: First, a specific radiochemical reaction must be suspected of relevance to a given biological effect. Second, if the reaction is known only *in vitro*, it must be proved to take place in the irradiated cell[7] and, moreover, it must occur *before* the biological effect. Third, if the reaction passes the foregoing preliminary tests, it must be *connected* with the biological effect.

The first of these three steps is comparatively easy and has been taken many times. In practically every case where a known cellular constituent has been altered by irradiation *in vitro*, this reaction has been suspected of relevance to biological effects. The second step is much more difficult, because it involves qualitative chemical analysis in the intact cell. However, it does not appear entirely hopeless; we may take encouragement from work such as that of Caspersson (1), who analyzes for such substances as proteins and nucleic acids in the intact cell.

The third step is perhaps the most difficult. By what procedure can connection be demonstrated? In general, there would seem to be a direct method and an indirect one. Given an indefinite amount of time, the direct approach might work. It consists of working out in detail the history of the molecules in the cell from the moment of absorption of radiation to the time of observation of the effect. This obviously is the desirable way to do it because, not only is connection proved, but the entire mechanism of radiobiological action is revealed. However, such a method involves technics and a knowledge of cell chemistry and physics which are unavailable today and probably for many years to come. In fact, today the chance of using this method appears fantastically improbable.

On the other hand, connection might be established with a fairly high probability by an indirect method. If, by a variety of means, the dose required to produce a given degree of the observed biological effect can be varied to a readily measurable extent, and if the yield of the radiochemical reaction can be shown to vary, both in direction and extent, in a manner consistent with its being the causation of the biological effect, then we may deduce that connection has been established with a reasonable degree of probability—at least with probability sufficient to justify the risk of further experimental time and effort.

Let us consider an example of the application of the above three steps in establishing relevance. It was early suspected that alteration of proteins might be relevant to biological effects, and when irradiation of certain protein solutions *in vitro* (6, 22) resulted in flocculation, the first step had been accomplished; a reaction known to occur *in vitro* was plausibly suspected of relevance. So far as I know, nobody has yet demonstrated flocculation of proteins in the cell; the second step is accordingly not yet accomplished. Nevertheless, a beginning has been made on the third step. When, during irradiation, the intracellular *p*H of *Drosophila* eggs or germinating fern spores (24) is modified in graded fashion by exposure to various concentrations of penetrating acids and bases such as carbon dioxide, hydrogen sulfide, and ammonia, it is found that their radiosensitivity exhibits maxima at definite concentrations of acid or base. This behavior has a striking resemblance to that of proteins *in vitro* because their

[7] If the relevant reactions occur in the medium rather than in the cell, the general argument is unchanged.

flocculation is maximal when the *p*H of the medium is kept at or near the isoelectric point during irradiation. Here is a crude beginning of the third step, the biological effect and the suspected radiochemical reaction being connected by virtue of the observation that the dose-effect relations are changed in the same unusual fashion by graded alteration of the same experimental factor. The third step is, of course, far from satisfactorily complete; connection needs to be demonstrated by altering the dose-effect relations by changes in other experimental conditions such as dose rate, specific ionization, temperature, etc. Moreover, the third step cannot be completed until the second step—demonstration of radiochemical flocculation in the cell—has been accomplished.

As investigation proceeds as indicated above, it may well result, in this instance, in a proof of irrelevance rather than of relevance. Nevertheless, the example given illustrates the sort of laborious procedure which may be used in arriving at an understanding of the mechanisms of radiobiological actions.

Today, with ionizing radiations becoming more and more prominent as a factor in our everyday environment, it is vital that we come to understand these mechanisms. It is evident that the difficulty of our attaining such understanding is indeed formidable, yet it is not necessarily discouraging. It is, indeed, extremely gratifying to see the present surge in radiobiological research in this country and elsewhere. At present our chief handicap in this research is shortage of personnel, especially of certain types. We have never had enough physicists in radiobiology and we are shorter than ever today, considering the increase in radiobiological effort. Moreover, it is now evident that if we are to work out the radiobiological mechanisms, we must have chemists. At present there are scarcely any in the field. Somehow, the important opportunities in radiobiology must be brought to the attention not only of biochemists but also of physical and organic chemists.

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SUMARIO

Relaciones entre los Efectos Químicos y Biológicos de la Radiación Yonizante

Como el protoplasma es un sistema acuoso, la química de la irradiación de las soluciones acuosas reviste interés particular por la luz que puede lanzar sobre los mecanismos de los efectos radiobiológicos. Ciertos fenómenos, tales como el efecto de dilución y el efecto de "protección," observados comúnmente en las soluciones acuosas irradiadas de sustancias inorgánicas y orgánicas simples, han sido también observados después de la irradiación de soluciones de enzimas y virus y de suspensiones de células aisladas. Además, ciertos factores experimentales, tales como el *p*H y la yonización específica, afectan de modo semejante la efectividad química y biológica de las radiaciones yonizantes.

Es importante llevar los aportes de la radiobiología al conocimiento, no sólo de los bioquímicos, sino también de los fisio- y los organoquímicos.

Structural Differences in Bone Matrix Associated with Metabolized Radium[1]

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THE METABOLISM of radium in the body has been a matter of concern since attention was first directed to radium poisoning by Blum (1) and Martland (2). Subsequent investigations (3, 4) have confirmed early suggestions that radium absorbed by an animal is eventually deposited in the skeleton. A few autoradiograms of human and experimental animal bones have shown that the radium is not uniformly distributed, but no quantitative measurements of its distribution have been published. Considerable uncertainty as to radium tolerance exists because of the dearth of quantitative data associated with observable physiological effects. So far as is known, no suitable rapid method of preparing the hundreds of bone sections necessary for such studies has been developed. The advent of nuclear energy and the possibility of human radioactive contamination have served to emphasize the need for such studies and for technics by means of which they can be made.

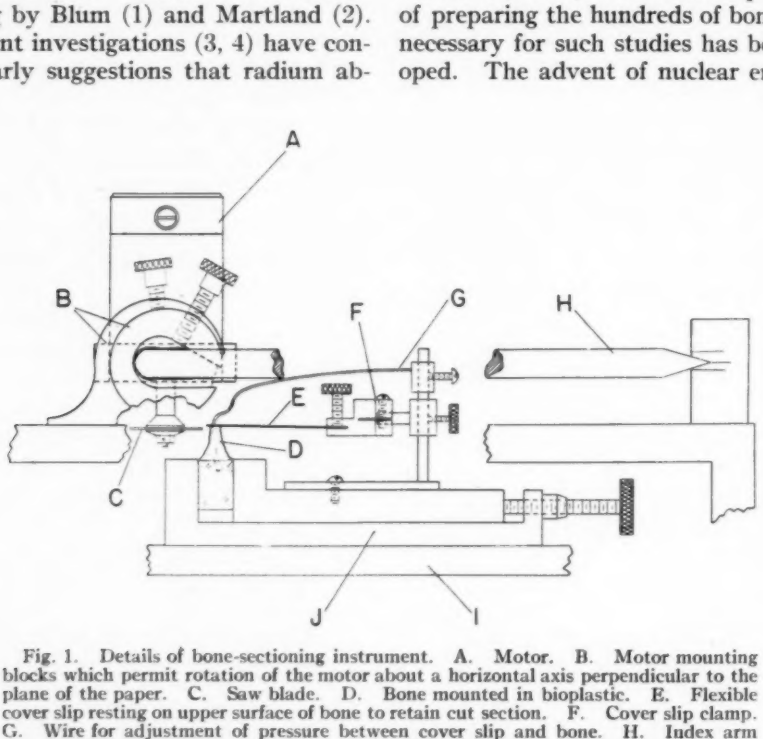

Fig. 1. Details of bone-sectioning instrument. A. Motor. B. Motor mounting blocks which permit rotation of the motor about a horizontal axis perpendicular to the plane of the paper. C. Saw blade. D. Bone mounted in bioplastic. E. Flexible cover slip resting on upper surface of bone to retain cut section. F. Cover slip clamp. G. Wire for adjustment of pressure between cover slip and bone. H. Index arm for adjustment of attack angle of saw. I. Carriage way. J. Bone carriage.

This paper presents preliminary results of studies of the distribution of radium in certain rat bones containing metabolically deposited radium. It describes, also, re-

[1] Presented at the Thirty-fourth Annual Meeting of the Radiological Society of North America, San Francisco, Calif., Dec. 5–10, 1948.

cently developed bone sectioning and autoradiographic technics which greatly facilitate the study of the distribution of radioactive substances in bone.

Material for study was prepared by intraperitoneal injection of radium chloride in physiological saline into 12-week-old Wistar rats. The distribution of the radium which was metabolically deposited in the bones of these rats was studied autoradiographically through alpha-particle tracks in nuclear track plates (Eastman NTB). So far, tibias and femurs have been chiefly studied. The matrix of these bones has been examined microscopically and photomicrographically for changes in structure and for differentiated areas associated with radium deposits.

EXPERIMENTAL TECHNICS

The microscopic investigation of radium distribution in bone and its relation to the cellular structure of the bone matrix required the development of a new method of bone sectioning. Such studies demand the examination of hundreds—perhaps thousands—of bone sections. Older methods of preparation were much too slow and laborious. Moreover, in many cases bones from animals as much as two years old were studied, and the method described by Axelrod (5) is not easily applicable to old bone.

(*1*) *Bone Sectioning Method:* To eliminate the difficulties mentioned above, a method of cutting sections of uniform thickness, thin enough for microscopic and photomicrographic examination, has been developed. A small circular saw blade an inch in diameter and 150 microns thick, mounted on the shaft of a small, variable speed motor, was substituted for the knife blade on a brain microtome. Figure 1 is a diagram of the essential constructional features, while Figure 2 is a photograph of the instrument.

Several precautions must be taken in order to ensure uniform thickness of cut sections. The motor armature must be ball-bearing mounted to prevent end play, and the motor mounting must be very heavy to ensure rigidity. In addition, the motor mounting must permit a small amount of rotation of the motor about a horizontal axis perpendicular to the direction of motion of the bone carriage. This must provide a very rigid but fine adjustment of the angle of attack of the saw blade, in order to eliminate any tendency on its part to cut out of or too deeply into the bone.

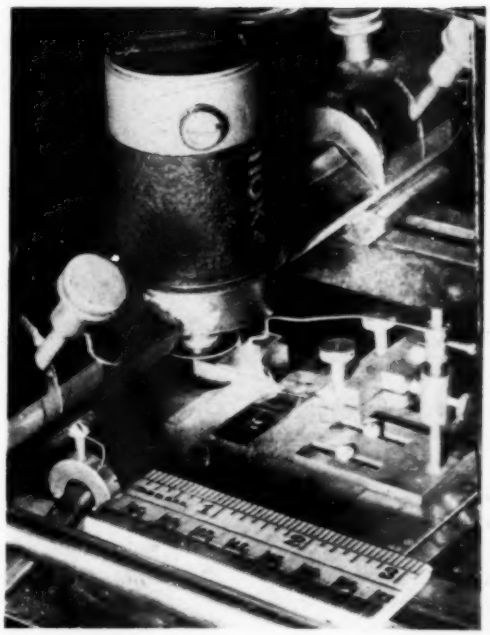

Fig. 2. Bone-sectioning apparatus showing motor mounting and arrangement for clamping flexible plastic cover slip in contact with upper end of bone.

The bone to be sectioned was embedded in bioplastic. After this material solidified, it was trimmed by means of a hand grinding tool so as to leave a thin shell of bioplastic surrounding the bone. A portion of the bioplastic extending beyond the end of the bone was left in the form of a block to permit clamping in the movable carriage of the microtome. The carriage was then moved in the conventional manner, but much more slowly, so as to feed the bone to the saw. The speed of the saw was controlled by means of a variable transformer. The cut section was retained on the lower side of a plastic cover slip,

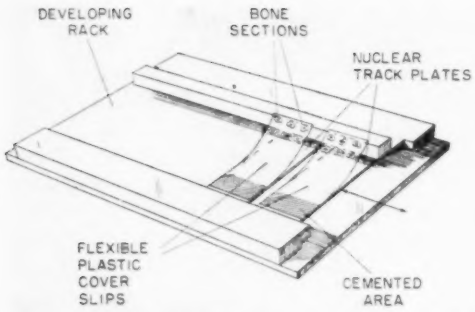

Fig. 3. Detail of nuclear track plate developing rack made entirely of lucite.

one end of which was clamped to the microtome carriage in such a manner that the opposite end rested on the squared end of the bone which formed the upper side of the cut section.

Sections may be cut in this manner at the rate of at least one a minute. Serial sections may be cut along the full length of the bone, with the loss of only about 150 microns of bone between sections. These are of uniform thickness, which may be as little as 30 microns. Figure 6 is a photomicrogram of a typical bone section cut by this method.

(*2*) *Autoradiographic Method:* The correlation of radium distribution in each bone section with the structural details of the matrix necessitated the development of a special autoradiographic technic, which permitted exact registry to be retained between the alpha-particle track image of the radium distribution and the alpha-particle sources in the bone section. This problem was greatly magnified by the necessity of removing the bone sections from the nuclear track plate after exposure to permit developing solutions to reach the emulsion under the section and to avoid immersing the section in the solutions. It was found desirable, also, to remove the bone section for photomicrographic purposes. It then had to be returned to *exactly* the position it occupied on the nuclear track plate during exposure.

These requirements were met by mounting six or eight bone sections at the end of one side of a transparent plastic cover slip. The opposite end of this cover slip was then cemented to the emulsion side of a nuclear track plate with the bone sections in contact with the emulsion. The sections were pressed in intimate contact with the emulsion during exposure.

At the end of the exposure period, the nuclear track plate with attached cover slip was placed in a plastic developing rack, as shown in Figure 3. The end of the flexible cover slip to which the bone sections were attached was lifted away from the emulsion and held above the surface of the developing solutions by the rail until the development process was completed.

Following development, the bone sections and their respective autoradiograms were examined microscopically. Photomicrographs of interesting fields in the bone matrix and the associated alpha-particle tracks were made. The best photomicrographic results were obtained by lifting the end of the cover slip with attached bone sections away from the nuclear track and focusing the microscope directly on the alpha-particle tracks, as illustrated by Figure 4. The bone sections were then allowed to fall back to their original positions and the microscope was focused upon them.

Careful tests have been made to determine whether this method provides and maintains exact registry between the bone section and the alpha-particle image of the radium distribution. No evidence of slippage has been found.

RESULTS

While it has long been recognized that the radium distribution in the bone matrix is non-uniform, the variations to be expected in the volume density have not been known.

Possible understanding of the effects of radioactive substances deposited in bone depend upon knowledge of the manner in which the substance is deposited and of maximum volume densities to be found. This is true particularly as regards the mechanism by which bone sarcomas are

induced by radium. It has previously been assumed that the effects of radium in the body of an animal must necessarily be proportional to the total quantity fixed in the bones. This may be true as regards acute effects resulting in the development of anemia. It may not necessarily be true as regards the development of bone sarcomas usually associated with chronic radium poisoning.

Microscopic studies of alpha-particle autoradiograms in these experiments have disclosed minute localizations of radium at various points in the bone matrix and the periosteum which seem to bear no simple relationship to the total radium in the bones. One type of localization is illustrated by the alpha-particle autoradiogram of Figure 5. When this is compared with the photomicrogram of the bone section, reproduced in Figure 6, the high alpha-particle densities are observed to coincide with areas of increased optical density in the bone matrix. This coincidence may be more clearly shown by the composite photomicrogram of Figure 7, in which the autoradiogram and bone section have been superimposed in registry as during the original exposure.

Examination of large numbers of bone sections and their autoradiograms appears to affirm an invariable association of areas of optical density with localized concentrations of radium in the bone. It cannot be definitely stated, at this time, that there is a metabolic relation between the darkened areas and the localized radium deposits. If there is such a relationship, however, it appears that the radium is concentrated in this manner because of the presence of these differentiated areas rather than the reverse. This conclusion is based on the observation of differentiated areas unaccompanied by heavy deposits of radium. The microscopic details of the optically dense regions do not show well in the photomicrogram, but careful study seems to disclose a higher density of canaliculi in these areas.

Concentrated deposition of radium is observed to be associated with another type of differentiation in the bone matrix. This is illustrated by the autoradiogram of Figure 8 and by the accompanying bone

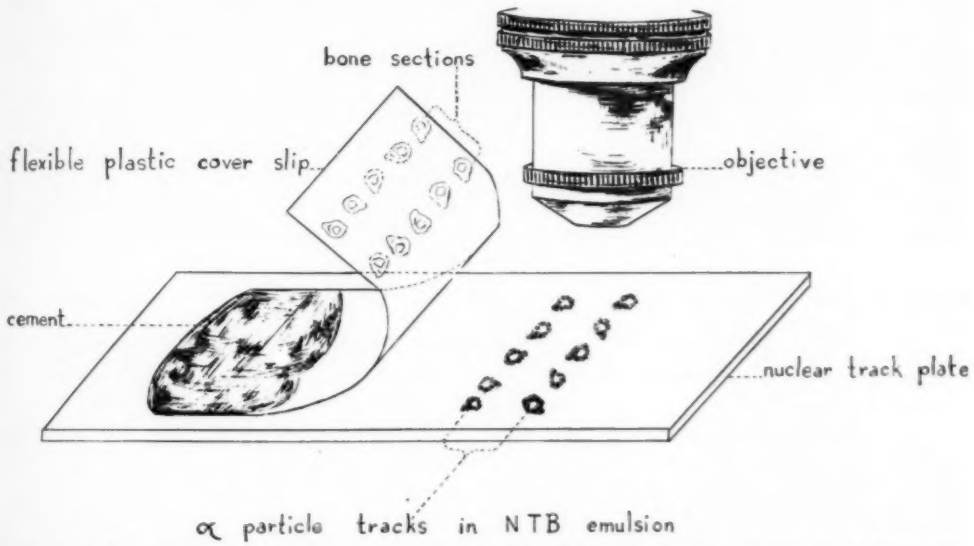

Fig. 4. Method of studying alpha-particle tracks on the nuclear track plates. This technic eliminates the necessity of focusing through the reverse side of the slide and interference due to passage of light through the bone section.

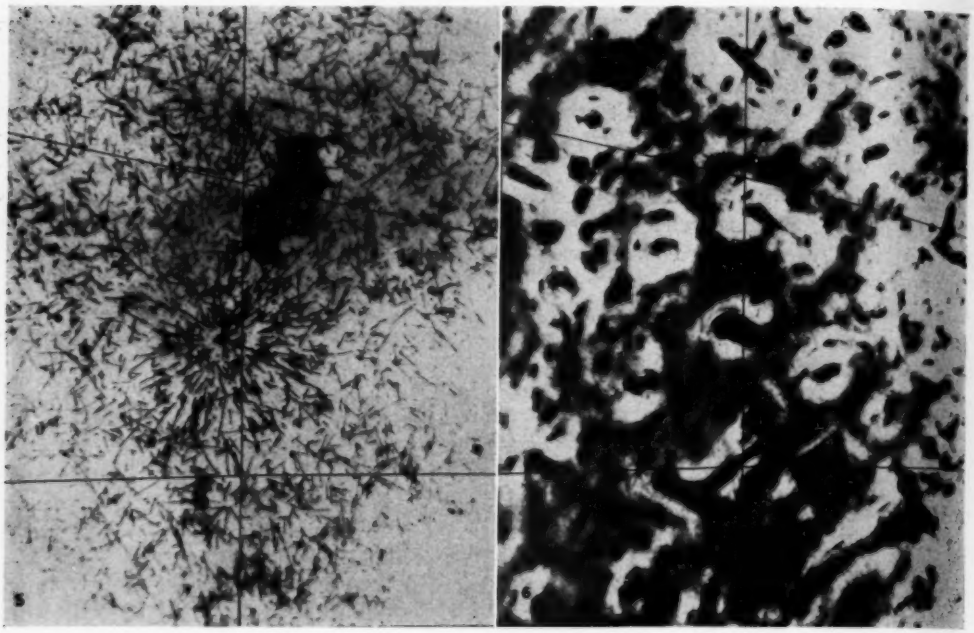

Fig. 5. Photomicrogram of alpha-particle track autoradiogram resulting from the presence of radium in a thin section of a rat tibia. Exposure, forty hours. The distance between points of intersection of horizontal lines with the vertical line is 180 microns.

Fig. 6. Photomicrogram of the portion of the bone section of which Fig. 5 is the autoradiogram. The rat from which this tibia was taken received 30 micrograms of radium chloride intraperitoneally at the age of twelve weeks and was sacrificed fourteen days after injection. Radium burden at death was 6.9 micrograms.

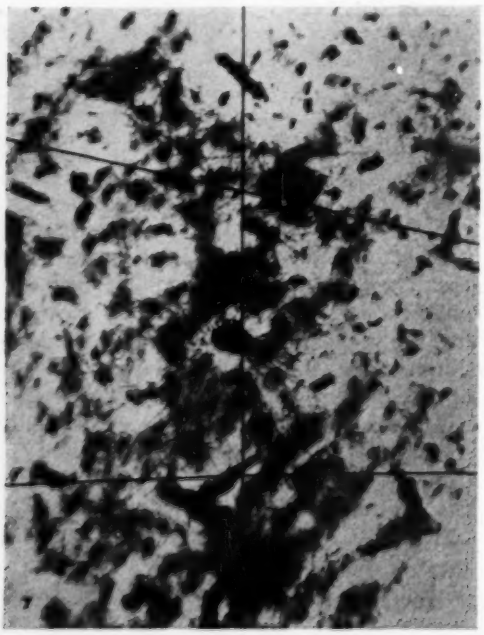

Fig. 7. Composite print of the negatives of Figs. 5 and 6 superimposed in exact registry, as during the autoradiographic exposure.

section, Figure 9. Here again a clearly defined differentiated line within the bone matrix is seen to be the site of heavy deposition of radium. In this case, however, the dense region in the bone appears to have resulted from the injection of the radium. The low-power photomicrogram of the bone section, Figure 10, shows a well defined line of high optical density which is approximately concentric with the marrow cavity. In this case, the radium had been injected when the rat was twelve weeks old, five months previous to the date of killing. The inner ring of seemingly normal matrix is believed to represent bone growth before the radium injection. The ring of differentiated bone is believed to have been laid down coincident with the deposition of the radium. This conclusion

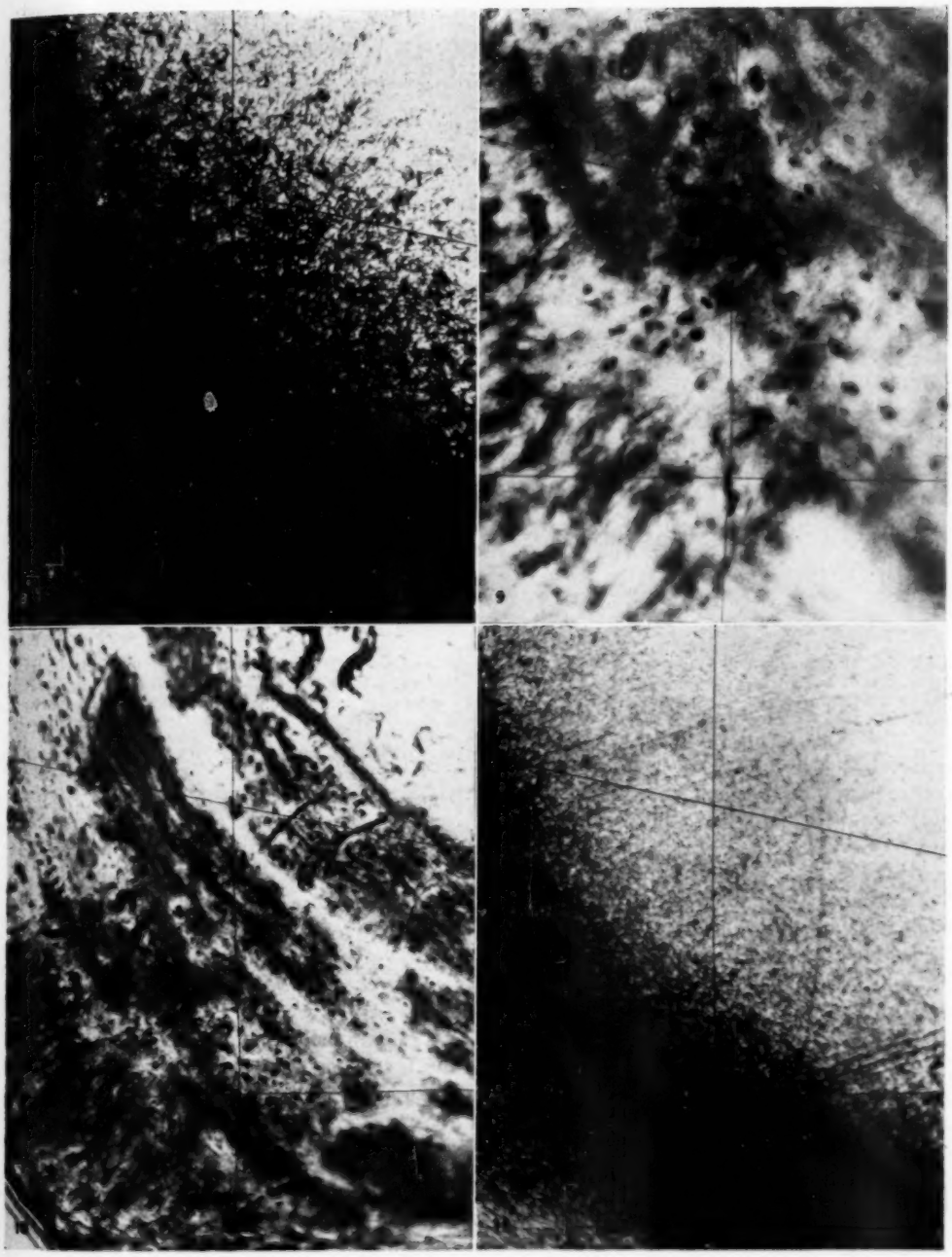

Fig. 8. Photomicrogram of a portion of an autoradiogram of a section of rat tibia. Exposure, forty-seven hours.
Fig. 9. Photomicrogram of the portion of the bone section of which Fig. 8 is the autoradiogram. This rat received 40 micrograms of radium chloride injected intraperitoneally at the age of twelve weeks and was sacrificed five months after injection.
Fig. 10. Low-power photomicrogram of a portion of the bone section of which a part is shown in Fig. 9.
Fig. 11. Low-power photomicrogram of the autoradiogram of the area of the bone section shown in Fig. 10.

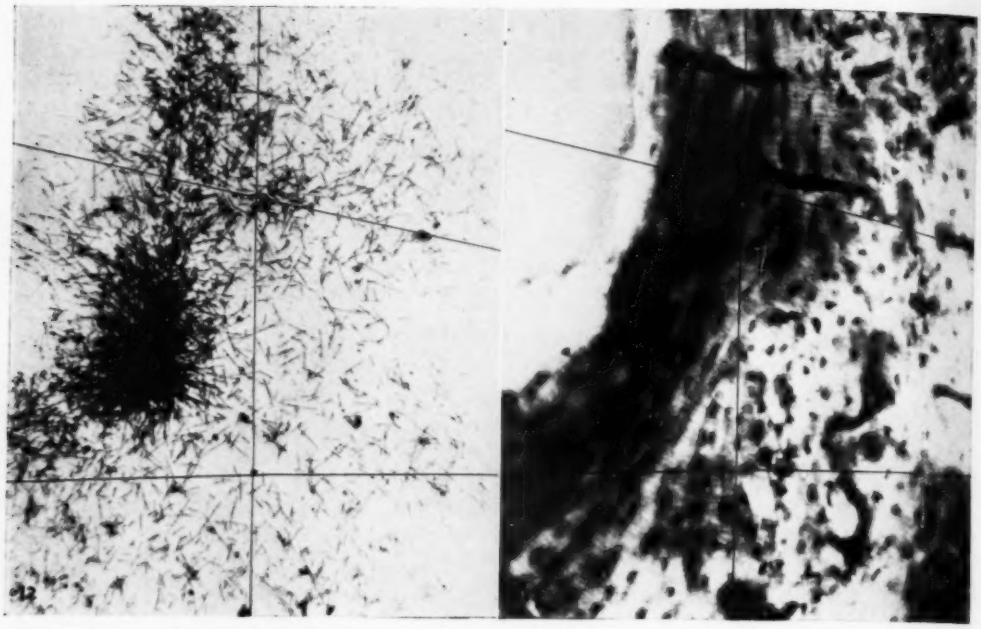

Fig. 12. Photomicrogram of a portion of an autoradiogram of a section of rat tibia. Exposure, forty hours.
Fig. 13. Photomicrogram of the portion of the section of rat tibia of which Fig. 12 is the autoradiogram. This animal received 30 micrograms of radium chloride at the age of twelve weeks and was sacrificed fourteen days after injection.

is based on the fact that the radium concentration, Figure 11, coincides *exactly* with this optically dense ring. Subsequent normal bone growth corresponds to the portion outside the dense ring.

Perhaps the most interesting localization is the type shown in Figure 12. The alpha-particle track pattern appears to emanate from a radioactive deposit in a region of very dense bone (Fig. 13) confined to an extremely small volume, estimated at 5×10^5 cubic microns. The tissue in the immediate region of a radium localization of this type must, of course, receive a very heavy bombardment by alpha particles. The ionization produced in any given minute volume of tissue during a reasonably long period of time, say twenty-four hours, will depend upon its location with respect to the radium deposit. Microscopically, this deposit does not appear to be a point source. On the other hand, the autoradiogram indicates that, as the center is approached, the number of alpha particles per unit volume increases rapidly. Consequently, it is extremely difficult to express the tissue dose due to alpha-particle bombardment in terms of roentgens or roentgen equivalents. The problem is complicated further by the high specific ionization due to alpha particles and the consequent greater biological effectiveness.

However, the average ion density may be estimated, and, when this is converted to roentgens on the basis of 1.62×10^{12} ion pairs per gram of tissue, some idea of the alpha-particle tissue dose may be obtained.

An estimate of the tissue dose due to the alpha particles has been made, as follows. A reduced (twelve-hour) autoradiographic exposure of this area was made. This resulted in an alpha-particle track density such that the tracks emanating radially from the localization area could easily be counted. An arbitrary circle of 25 microns radius was drawn about the center of the radium locus. Then all alpha-particle tracks which, when projected back toward the center, pass through this arbi-

trary circle are considered to originate from radium deposited within a volume of which this circular area is the great circle.

Since a means has not yet been devised for locating the saw cut with reference to the center of the deposit, it has been assumed, for purposes of this estimate, that the arbitrary circle coincides with the center of the deposit. Any error involved in this assumption tends to reduce the estimated dose. It is assumed further that the nuclear track plate has registered one-fourth of all the alpha particles emitted from the radium in this volume.

It seems reasonable that the maximum volume of bone in which these alpha particles would have expended their energies is a volume having as its radius the radius of the arbitrary circle plus the maximum range of an alpha particle in bone. This range is not known accurately but has been assumed to be 25 microns.

The total number of ion pairs produced by the alpha particles per gram of tissue has been calculated on the basis of the above assumptions. The approximate average tissue dose thus obtained for the radium locus of Figure 12 is 500 roentgens per twenty-four hours in the volume considered. It must, of course, be evident that many assumptions are involved in this estimate, which may have to be revised at a later date, but estimates made in other ways yield doses of nearly the same value.

Any tissue receiving such a dose would, of course, be killed. It seems, therefore, safe to assume that there will be a more or less spherical volume of tissue associated with this type of localized deposit which will be killed soon after the deposition of the radium. This volume of dead tissue would enlarge with time as the total cumulative dose at the boundary reached the lethal value. There will at all times be a surrounding volume of tissue which has received a sublethal dose, but which is subjected to continual bombardment.

A high incidence of osteogenic sarcoma has been repeatedly demonstrated in human victims of radium poisoning and in laboratory animals which have received radium by injection and otherwise. These sarcomas have been attributed to the presence of radium in the bones, although the precise manner in which the sarcomas might be induced has received little attention.

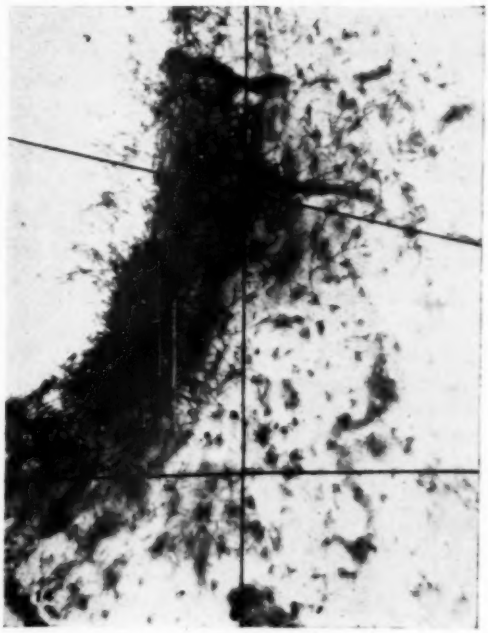

Fig. 14. Composite print of the negatives of Figs. 12 and 13 superimposed in exact registry, as during exposure.

These studies have demonstrated the existence of microscopic localizations of radium deposited metabolically in the bones of rats. Consideration of the tissue dose due to alpha-particle bombardment and the resultant tissue reaction in the sublethal dose border region may offer a reasonable basis for a theory of the production of bone sarcomas in chronic radium poisoning. Further studies along this line are being intensively pursued.

NOTE: This work has been sponsored by the Office of Naval Research under contract N6onr 260-T.O.-1.

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SUMARIO

Diferencias Histológicas en la Matriz Osea Asociada con el Radio Metabolizado

Los siguientes son los resultados preliminares de los estudios de la distribución del radio en ciertos huesos de ratas que contenían radio depositado metabólicamente. Después de inyectar cloruro de radio en suero fisiológico en las ratas, se determinó autorradiográficamente la distribución del radio en los huesos rastreando las partículas alfa en placas de trazos nucleares (NTB Eastman). La matriz ósea fué estudiada microscópica y microfotográficamente en busca de alteraciones histológicas y de zonas diferenciadas asociadas a los depósitos de radio. Para este fin se introdujo una técnica especial de cortes de huesos, así como una técnica autorradiográfica *ad hoc*, que permite retener la relación exacta entre la imagen de los rastros de partículas alfa del radio distribuído y los focos de partículas alfa en el corte óseo.

El examen de grandes cantidades de cortes óseos y de sus autorradiografías pareció establecer una asociación invariable de zonas de densidad óptica con concentraciones localizadas de radio en el hueso. Por ahora, no cabe afirmar positivamente que exista relación metabólica entre las zonas oscurecidas y los depósitos de radio. Sin embargo. de existir dicha relación, parece que el radio se concentra en dicha forma debido a la presencia de dichas zonas diferenciadas, más bien que lo contrario.

Dedúcese que el estudio de la dosis histológica debida al bombardeo por partículas alfa y la consiguente reacción histológica en la región colindante con la dosis subletal puede aportar una base lógica para una teoría de la producción de osteosarcomas en la intoxicación crónica con radio. Los estudios en este sentido prosiguen intensamente.

DISCUSSION

(Papers by Jacobson, Marks, and Lorenz, in March issue, p. 371; Zirkle; Hoecker and Roofe)

Titus C. Evans Ph.D. (Iowa City, Iowa): The report by Dr. Jacobson is very interesting, but somewhat disturbing. The reasoning on which most radiotherapy is based is that rapidly multiplying immature cells are more radiosensitive than mature and mitotically inactive ones. It might be concluded from the data just presented that the above generalization is in error. I believe that we should keep an open mind until we decide whether these results indicate an exception to the general rule, a new phenomenon, a confusion of terminology, or an incomplete picture.

As regards terminology, it seems that we must decide whether radioresistance means that few cells are destroyed or that many cells survive. In Dr. Jacobson's experiments, the number of cells present during or soon after irradiation is increased by certain stimuli. About as many cells in the hyperplastic marrow survive a certain radiation exposure as survive in bone marrow irradiated without the growth stimulus. However, more cells have been destroyed in the case of the hyperplastic marrow. Now, let us compare two cases of lymphoid leukemia: One patient has a white cell count of 200,000, which, after a relatively small dose, is reduced to say 8,000. This is a tremendous effect. In another patient, a blood count of let us say 18,000 is reduced by the amount of radiation to perhaps 4,000. The relative effect has been much greater in the case of the very hyperplastic leukemia, yet the appearance of the bone marrow in the latter case must have indicated that there were fewer residual cells.

If it turns out that experimental modification of cell number at the time of irradiation affects the percentage of cells surviving, then it would appear that the chief radiation effect was an indirect one. If, however, the effect is indirect, then a certain number of molecules of a toxic material would be produced; a

number of cells would be affected; and the percentage effect would depend on whether we had one or a hundred cells per molecule of the poison. Such indirect effects may be due to "activated water," hydrogen peroxide, or histamine-like substances.

A third possibility is that, under the additional stimulus, surviving cells are able to regenerate the bone marrow more rapidly than usual. There are many very interesting problems in connection with this study, and I am sure that Dr. Jacobson will not stop at this point but will carry his experiments on even more extensively.

As to Dr. Zirkle's paper, I feel that I should mention that we all recognize the important role played by his study of the effects of alpha particles. We have become aware of the effect of specific ionization, and those who used to argue about the effects of wave lengths have been brought to a better understanding of this subject because of this type of work.

One is tempted, in a study of effects on cells in a suspension, to attribute some importance to effects produced, not on the cells themselves, but in the water molecules which indirectly affect the cells. The work is too detailed to go into at this time. The exposures required to demonstrate "activated water" are higher than the usual therapeutic range.

One of the poisons produced that can be identified is hydrogen peroxide, and we are interested in knowing if hydrogen peroxide could account for the entire biological effect. We have found that it does not. If we increase the exposure tremendously, we are able to produce enough hydrogen peroxide in the water to have, in turn, an effect on the cells that have themselves been unirradiated. Not only will the hydrogen peroxide eventually kill the cells, but it will affect cell division. Now, one of the main things that has kept our feet on the ground regarding hydrogen peroxide, I believe, is that we are all aware that there is an enzyme in the cells called catalase, whose apparent function is to destroy hydrogen peroxide. It is supposed that this is perhaps the only function of this enzyme in the cell metabolism. It is there to destroy the hydrogen peroxide normally produced during the process of respiration, so that it will not be toxic. Therefore, in supposing that radiation might have a basic effect on cells in the production of hydrogen peroxide, one would have to assume that radiation would destroy the catalase. Some of us have attempted to learn something about this. We irradiated the catalase after it had been extracted from the cells and found that it was very radiosensitive in dilute solutions, as Dr. Zirkle has indicated. It was more resistant in concentrated solutions. Addition of albumin, for example, would protect the enzyme even in dilute suspensions. However, if we irradiated the cells and then extracted the irradiated catalase, we found only a slight effect, and this effect was not increased with increase in dosage. As we increased the exposure time, we would increase the number of cells destroyed, as well as the delay in cleavage, so that these effects and that of catalase destruction were not at all parallel. We are at a loss to explain the effects, even though there are certain similarities. It must be that there is something more basic; that the general effect is one of oxidation, similar in a general way to the action of hydrogen peroxide.

This particular poison, however, is only one of many possible agents, and I might say in passing that we are very interested in the findings indicating that certain enzymes are very sensitive—these nucleic acid studies, etc. What worries me most is that most of these effects are temporary, while the effects that we see in the cells are continuous and are continually growing worse, from the standpoint of increasing entropy or loss of potential energy, so that eventually the cell seems to wear out.

I think Dr. Hoecker has demonstrated that he has the technic which will give him the information that he is after, and I believe that it has already given some information on this subject. The dense areas which he describes are very interesting. It would be of value to know whether they represent affected areas or whether they exist normally and are regions with a particular affinity for radium.

Individualizing the Tumor Dose in Carcinoma of the Uterine Cervix by Means of a Simple Caliper[1]

JOSEPH B. JARVIS, M.D.
Tacoma, Wash.

IT IS THE PURPOSE of this paper to present a new instrument, a simple caliper, which is believed to offer an accurate, rapid, and convenient method of individualized treatment of carcinoma of the uterine cervix, based on actual tumor dose. This caliper permits direct skin-to-cervix measurement. While the method is admittedly less precise than some of the more elaborate technics described in the literature, it does offer, especially to the busy radiologist with limited personnel and equipment, a procedure whereby the entire treatment plan in any individual case may be worked out in a matter of minutes.

The accompanying illustration (Fig. 1) demonstrates the general features of the instrument. One rod—the vaginal piece—has a straight, free shaft which is calibrated linearly in centimeters from the tip. An obtuse angle (about 120 degrees) near the hub permits easier use for posterior measurements. The other rod is curved throughout its length to give clearance to the body parts. The centimeter calibration on the flat pieces is shown on both sides of the caliper for convenience.

The purpose of the centimeter scale on the straight rod is to obtain a measurement of the cephalad location of the cervix beneath the anterior abdominal wall in relation to the inferior margin of the pubic symphysis, establishing the cephalad-caudad position of the treatment field. This linear calibration is of no value for determining the cephalad-caudad location of the posterior treatment fields, since there is no bony landmark immediately posterior to the vagina to serve as a guide, and the bony contour in this region does not permit localization by this means. The posterior fields are measured to the center of the sacrosciatic notches.

The caliper is used in the following manner: The patient is prepared for pelvic examination in the usual position. The examiner introduces the straight rod into the vagina, guiding its tip to the cervical os (or lesion) with the fingers of one hand. While this tip is kept accurately in contact with the os during all measurements, the other hand swings the curved rod into position on the skin surface of the abdomen at the approximate center of the treatment fields to be used, and the operator reads the distance between the opened tips, which corresponds precisely to the thickness of the tissues traversed by the incident central beam of radiation in reaching the cervix.

The anterior measurements are made with the patient supine, preferably with the thighs not flexed, so that the anatomical relationship will correspond as nearly as possible to that which exists during treatment. The posterior measurements are best made with the patient prone, but, if the examining table in use does not allow a prone position suitable for the procedure, the patient can be turned to the left side for the right posterior and to the right side for the left posterior measurements. A direct lateral measurement can be made by having the patient flex the thighs so that the curved rod can be brought laterally in the horizontal plane of the cervix. After all of the desired measurements from the skin surface (at the center of the treatment fields) to the os have been obtained, standard depth dose tables are consulted, and a treatment plan based on actual tumor dose (cervix dose) is calculated in the manner described by Camiel and Blatz.

Since the measurements obtained correspond essentially to the "effective depth" as defined by Camiel and Blatz, their system of dosage calculation is employed to

[1] Accepted for publication in April 1948.

determine the number of treatments needed for each field in order to obtain a predetermined tumor dose. Depth dose tables readily indicate the "effective dose" per 100 r in air at each field. The desired tumor dose is then divided by the sum of the "effective doses" to find the number of treatments needed for each field.

For example, let us suppose the following measurements were obtained: two anterior oblique fields 13 cm.; two posterior oblique fields 15 cm.; two direct lateral fields 15 cm. The effective dose per 100 r in air is 33 r for the anterior oblique, 27 r for the posterior oblique, and 27 r for the direct lateral fields, at 200 kv.p., with 0.5 mm. Cu plus 1.0 mm. Al filtration, 50 cm. target-skin distance, and 10 × 15-cm. fields.[2] The sum of the effective doses for a single cycle is 174 r (33 r × 2 plus 27 r × 4). If 200 r in air are to be given to each field, then the effective dose at this rate is 348 r (174 r × 2). Let N be the number of treatments needed for each field when a total tumor dose of 4,000 r is desired and we see that

$$N = \frac{\text{desired tumor dose}}{\text{sum of effective doses}} = \frac{4{,}000\,\text{r}}{348\,\text{r}} = 11.5 \text{ treatments.}$$

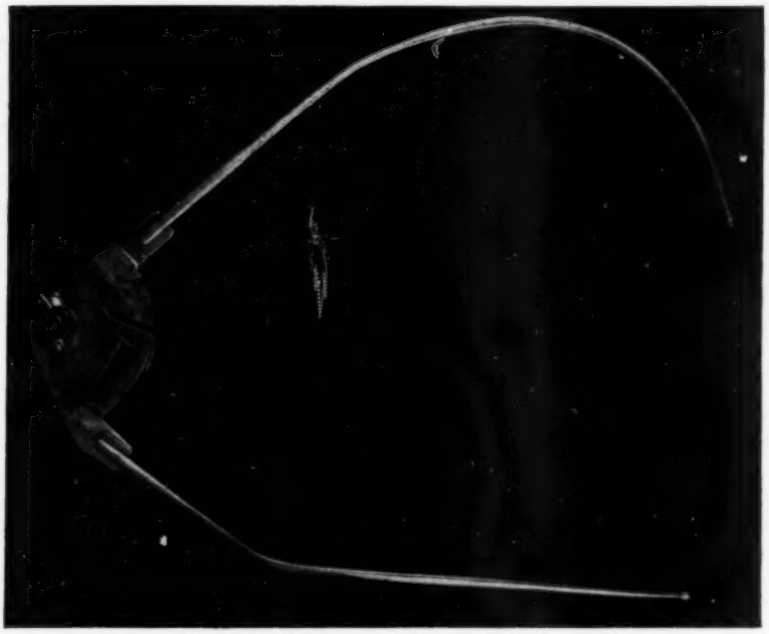

Fig. 1. Showing the essential features of the caliper. The straight (vaginal) rod is calibrated in centimeters along its inner surface. Each of the calibration lines on the flat piece indicates one centimeter; each five centimeters are emphasized by longer lines and figures.

Twelve treatments would give a tumor dose of 4,176 r.

With this method of determining the cervix depth from the center of oblique treatment fields, it is not at all uncommon to find the measurements to be in excess of 10 cm. So slight a thickness has been encountered only in the small, frail patient. It is likely, therefore, that most patients should be treated through more than four fields and that those having measurements in excess of 13 cm. should be given air doses of more than 200 r per treatment in order to complete the series

[2] Depth dose for 10 × 15 cm. field obtained by interpolation.

in approximately four weeks. The higher skin doses probably can be tolerated well, since the greater number of fields will permit a longer recovery period between treatments administered to the same field. It is also likely that those patients having measurements greater than 15 cm. should have the external irradiation divided into two courses at intervals of two to three months, with intracavity radium application during the rest period.

It is realized that external irradiation is only one of the radiologist's methods of treatment, and that, especially in patients of great thickness, the other technics (radium and transvaginal roentgen therapy) must be utilized in a coordinated manner in order to reach the goal of a full, cancerocidal dose to the primary lesion and its advancing extensions. It is hoped that this caliper may play a part in the evolution of an irradiation attack whereby there may be delivered to every neoplastic cell in the cervix, pelvic ligaments, and regional lymph channels a lethal injury without exceeding the tolerance limit of the patient.

It is possible that a similar caliper on a smaller scale might be useful in determination of the depth dose in other accessible orifices, such as the mouth.

SUMMARY

A simple caliper is described for assistance in accurate, individualized determination of the actual tumor dose in carcinoma of the cervix.

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REFERENCE

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SUMARIO

La Individualización de la Dosis Tumor en el Carcinoma del Cuello Uterino por Medio de un Sencillo Compás

El sencillo compás aquí descrito ayuda a individualizar la dosis tumor en la irradiación externa por carcinoma del cuello uterino. Introducida una rama del compás en la vagina y mantenido el extremo en contacto con la boca cervical (o la lesión), la otra, encorvada adecuadamente (véase el grabado), es girada a su posición en la cara del abdomen en el centro aproximado de los campos predeterminados para tratamiento. Luego se lee en una escala calibrada la distancia entre las dos puntas del compás, correspondiendo la misma al espesor de los tejidos que tiene que atravesar el haz de rayos X para alcanzar el cuello.

Después de determinar las mediciones deseadas de los varios campos, se consultan tablas guías para la dosis y la profundidad y puede trazarse un plan terapéutico basado en la real dosis tumor.

Effects of Continuous Radiation on Chick Embryos and Developing Chicks[1]

II. Bone Marrow, Lymphoid Tissue, and Peripheral Blood

SHIELDS WARREN, M.D., and FRANK J. DIXON, M.D.

THE FOLLOWING description of the effects of lethal and sublethal continuous radiation on the bone marrow, lymphoid tissue, and blood of chick embryos and developing chicks, by means of the isotope P^{32}, is the second part of a study embracing all the tissues in these subjects and including measurements of the localization of the agent within the tissues (2).

The findings described in the first report were briefly as follows:

Radiation caused an over-all growth retardation resulting in small but well proportioned birds.

Both testes and ovaries were very radiosensitive, the primitive germ cells being the most sensitive element. The spermatogenic cells of the testes remained extremely sensitive to radiation throughout their development, while the ova became more radioresistant as they matured.

Bone growth was retarded by radiation. The cartilage cells of the epiphyses were much more radiosensitive than the osteoblasts and osteoclasts. After irradiation ceased, the histologic changes were reversible and the bones regained a normal histologic structure but remained dwarfed.

MATERIALS AND METHODS

P^{32} combined as KH_2PO_4 was injected into eggs which were incubated under the usual conditions of 38–39° C. and 70–80 per cent relative humidity. The incubated eggs were divided into groups according to the amount and time of injection. Injections varied in amount from 47.5 μc to 300 μc. At regular intervals embryos and birds were selected at random from each group, killed by decapitation, and studied histologically.

In order to study radiation effects later in the course of development, subcutaneous injections of approximately isotonic solution of P^{32} as KH_2PO_4 were made into twenty-four chicks after hatching. Doses varied from those producing no histologically demonstrable effects to those causing death. The smallest dose was 115 μc, the largest 3,696 μc.

EFFECT OF RADIATION ON BONE MARROW

Radiation had its crucial effect on the blood-forming tissues. The concentration of the radioactive substance within the bones caused heavier irradiation of bone marrow than of other tissues.

Hematopoiesis takes place during the early part of incubation, largely in the blood islands of the vitelline sac. Between the tenth and twelfth day of incubation, the bone marrow begins its hematopoietic function, and several days before hatching it is the chief source of red blood cells and granulocytes. Blood-forming marrow develops in all bones, but the greatest number of hematopoietic cells is found in the long bones and vertebral bodies. The liver and spleen do not appear to be of importance in hematopoiesis in the embryo or young chick.

Erythrocytes form within endothelial-lined sinuses of the bone marrow, apparently in communication with the circulation, and enter the circulation when they are mature. Granulocytes are formed in the intersinusoidal spaces and after reaching maturity migrate into the circulation.

Hemocytoblasts, apparently the stem

[1] This work was done under Government Contract N5-ori-76 in the Laboratory of Pathology of the Harvard Cancer Commission. P^{32} supplied by Oak Ridge National Laboratories. Accepted for publication in May 1948.

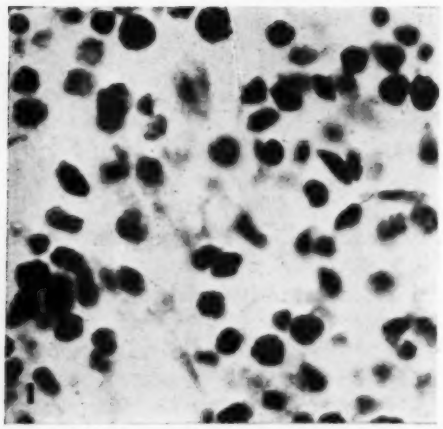


Fig. 1. Femoral marrow from eighteen-day embryo given 120 μc on fourth day of incubation. Marked depletion of marrow with increase in proportion of undifferentiated immature cells without signs of regeneration. Cells are irregularly scattered rather than in close-packed islands as in normal (Fig. 3). ×800

cells of both granulocytes and erythrocytes, are found in the marrow, but most of the mature cells are formed by multiplication of early forms which have already partially differentiated and are fixed in their line of development.

The range of normal counts determined from our control birds during their first two months of life is given on Graph I. The oval, nucleated, mature erythrocytes of the chick measure approximately 12.2 μ × 7.3 μ and contain hemoglobin in their cytoplasm. There are heterophilic, eosinophilic, and basophilic granulocytes which correspond roughly in appearance and relative frequency to their human analogues. Lymphocytes resemble human lymphocytes and are the most numerous of the leukocytes.

Study of the platelets and the altered clotting mechanism of the blood of these irradiated chicks will be the subject of a subsequent report.

Ectopic hematopoiesis did not occur in any of our birds, even though many of them had marked pancytopenia and no myeloid hematopoiesis. There were no infectious processes seen in chicks with prolonged agranulocytosis and lymphopenia, such as commonly accompany similar blood pictures in mammals. There were numerous petechial hemorrhages on the serous surfaces and in the muscles and lymphoid tissues of the most anemic birds, and some pulmonary edema, but these findings were almost terminal.

Our observation covered a period of continued growth of the hematopoietic tissue. Routine bone-marrow samples were obtained from the tibia and femur, a cervical, a thoracic, and a lumbar vertebra, and the skull.

Sublethal continuous irradiation of embryos had two effects on the bone marrow: first, proper maturation of the immature hematopoietic cells was inhibited; second, mitotic activity was reduced. The effects on the granulocytic and red cell series were not consistently different.

In the embryos given 100 μc on the eighth or fourteenth day of incubation and those given 120 μc on the fourth day of incubation, the above effects were clearly seen and were most obvious in well calcified areas where the radiation was heaviest. An increase in the proportion of immature forms, especially in the red cell series, resulting from reduced maturation, was first evident within four days, reached a maximum in one week, and remained a striking feature of the marrow for several weeks. During the first several days of irradiation, these immature cells showed no evidence of injury and displayed some mitotic activity, but as radiation injury became more severe, the mitotic activity was greatly reduced, the number of marrow cells decreased, and the proportion of stem and blast forms increased. These cells did not appear able to develop into mature blood cells. In the period of most severe radiation injury, one to two weeks after injection, the marrow contained one-fourth to one-third the normal number of cells. Most of these were immature forms and many were deeply basophilic, irregular in size and shape, showing no mitoses (Fig. 1). Even at this time, however, the reticulo-endothelial cells appeared to be uninjured. Then, two to three weeks after injection, with

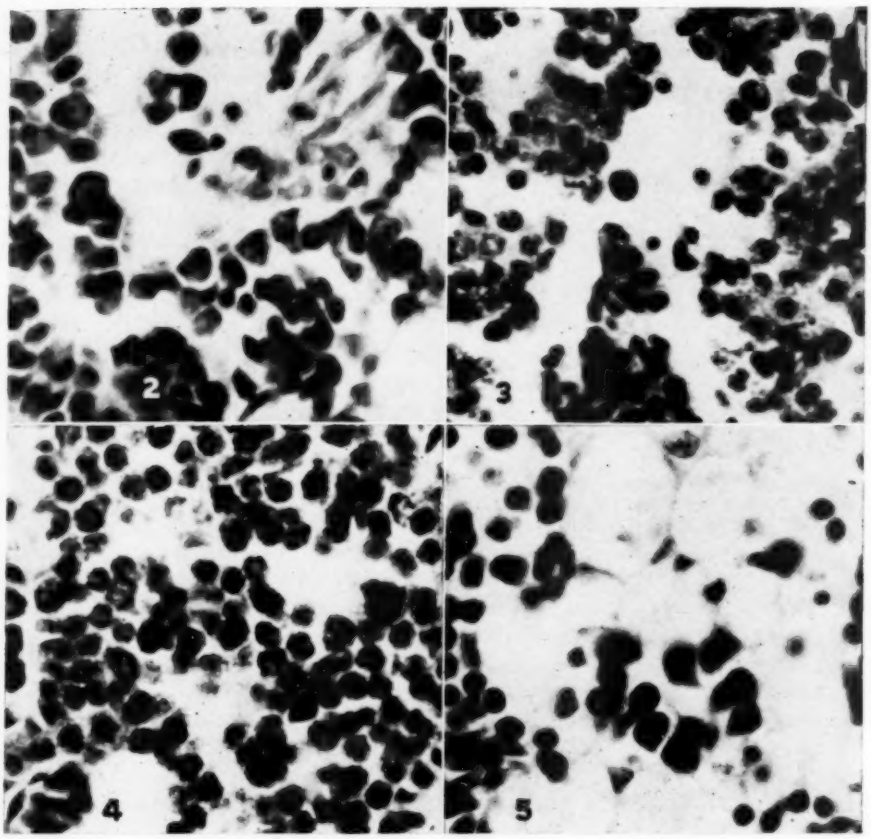


Fig. 2. Femoral marrow from hatching chick given 120 μc on fourth day of incubation. Undifferentiated, immature cells predominate and appear more active than three days previously (Fig. 1), but there is still little evidence of maturation. ×800

Fig. 3. Femoral marrow from normal hatching chick. Close-packed differentiating cells with only occasional immature forms make up the cords and islands of the marrow. (Compare with irradiated marrow, Figs. 1 and 2). ×800

Fig. 4. Femoral marrow from normal seven-day chick. Note close packing of cells, most of which are partially differentiated granulocytes. The reticulo-endothelial and stem cells are not apparent. ×800

Fig. 5. Femoral marrow from seven-day chick given 100 μc on fourteenth day of incubation. Active regeneration is evidenced by many large stem and blast forms, large reticulo-endothelial cells, and few irregular large, basophilic cells. Most of the cells are still very immature. Compare with normal seven-day marrow (Fig. 4), where very few of these early forms can be seen. ×800

disappearance of radiation, the marrow began to recover (Fig. 2) as the remaining immature cells first began to display mitotic activity and, several days later, maturation which resulted in the formation of normal adult cells. The reticulo-endothelial cells were larger than normal (Fig. 5) and in a few instances appeared to be differentiating into hematocytoblasts, an occurrence rarely if ever seen in normal hematopoiesis. Complete recovery of hematopoietic tissue followed, suggesting that no latent effects of radiation injury were operating in the first two months following irradiation. After recovery, these marrows showed occasional foci of small undifferentiated lymphoid cells, which were only rarely seen in unirradiated material. There was no regenerative hyperplasia of the marrow during our two to three month observation period following irradiation.

The effect of lethal amounts of constant

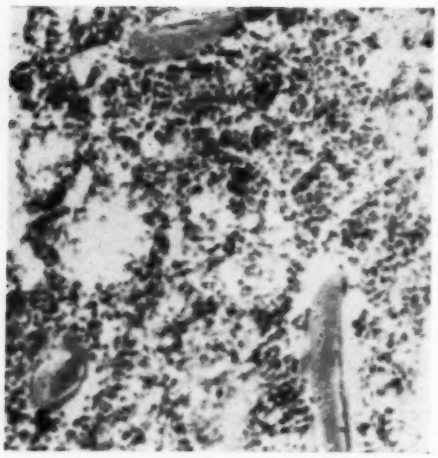


Fig. 6. Femoral marrow near lower epiphyseal line of normal seven-day chick. Marrow is well filled with close-packed, hematopoietic cells. ×200.

radiation (180 and 200 μc) on the embryonic bone marrow was significantly different from the effect of sublethal doses. Instead of a temporary inhibition of maturation and mitoses which resulted from the smaller doses, the larger doses promptly halted mitotic activity and maturation, as seen two to three days after injection. As the marrow cells were lost, they were not replaced, and after about one week of radiation, the number of marrow cells was reduced to one-third normal, but there was no increase in the proportion of immature forms, as seen with smaller doses. Many of the immature cells of both series were deeply basophilic, small, and irregular in shape. The reticulo-endothelial cells did not appear injured. After two weeks of irradiation, the marrow showed maximum injury (Fig. 7). Only a few hematopoietic cells remained, and they were basophilic, irregular and immature, but the reticulo-endothelial cells were still unchanged. The fat cells had undergone serous degeneration, with division of intercellular fat into numerous small droplets and the appearance of acidophilic granular protoplasm.

After two weeks, the level of residual radiation had apparently fallen below the point of suppression of mitosis and maturation and there were early signs of regeneration on the part of both the few remaining immature hematopoietic cells and the reticulo-endothelial cells (Figs. 8–10). There were scattered islands of stem and blast forms, which apparently had arisen from residual hematopoietic cells and were multiplying and undergoing some differentiation, although many of the cells of the red series were microcytic. The reticulo-endothelial cells were prominent and in several instances apparently gave rise to hematopoietic stem cells. This regeneration continued but was insufficient to prevent the development of a fatal pancytopenia several days later.

Discussion: The extent of the effect of radiation on the bone marrow depended on the amount given. Yet, regardless of the size of the dose, the same two basic effects were seen: first, inhibition of normal maturation; second, depression of mitotic activity. These two factors merely varied in degree in the different series of chicks previously described.

That these effects were only temporary, since apparently normal maturation and mitoses could be resumed after irradiation ceased, was well shown in these chicks. The sublethal radiation injuries of the marrow appeared to be completely reversible. Even the birds in which fatal anemia developed showed some regeneration on the part of the few remaining hematopoietic and reticulo-endothelial cells shortly before death, after radiation had decreased. This hematopoiesis, however, was not sufficient to maintain a blood count compatible with life.

The determining factor in recovery of the hematopoietic function after irradiation appeared to be the number of hematopoietic cells which escaped fatal radiation injury. Even though these cells may have appeared distinctly abnormal during the height of the radiation injury, at least some of those that remained seemed to resume normal appearance and function once radiation ceased. Also worthy of emphasis is the formation of hematopoietic cells from the reticulo-endothelial cells,

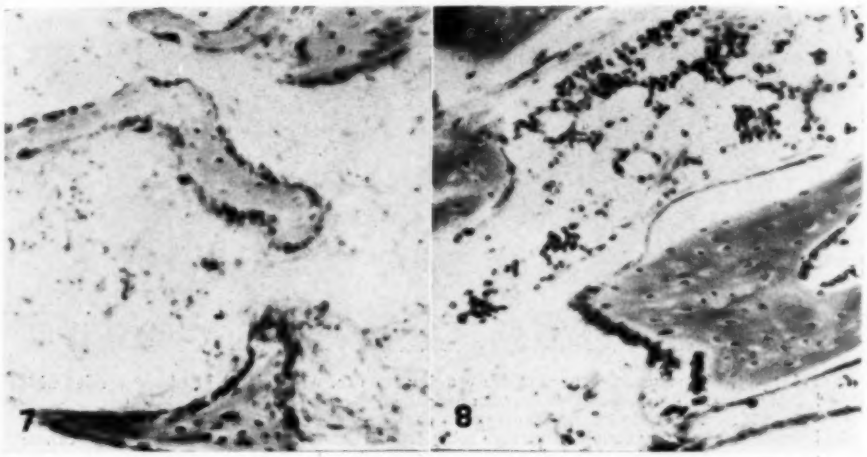


Fig. 7. Section near lower femoral epiphysis of seven-day-old chick given 200 μc on the fourteenth day of incubation. Almost no hematopoietic cells are present. Fat shows serous change. Compare with normal shown in Fig. 6. ×200

Fig. 8. Section near lower femoral epiphysis of eleven-day chick given 200 μc on fourteenth day of incubation. Early regeneration is evidenced by formation of small islands of hematopoietic cells. Compare with empty marrow of bird from same group examined four days earlier (Fig. 7). High-power view of these regenerating islands given in Fig. 10. ×200

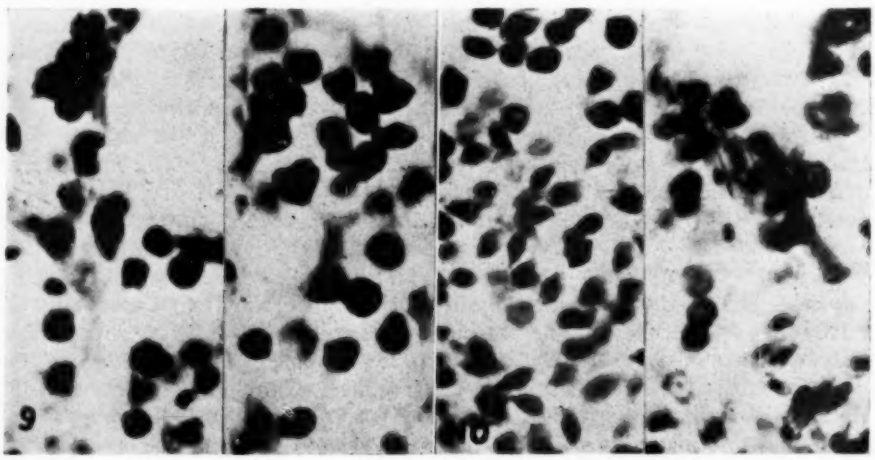


Fig. 9. Femoral marrow near lower epiphyseal line of nine-day chick given 200 μc on fourteenth day of incubation. Two islands of regenerating stem and blast forms show very slight maturation. Note mitotic figure near the lower part of the picture. ×800

Fig. 10. Femoral marrow near lower epiphyseal line of eleven-day chick given 200 μc on fourteenth day of incubation. Regenerating islands are larger than two days previously (Fig. 9). Some maturing cells (left) illustrate maturation, the second step in the marrow regeneration. Lower magnification of this marrow is shown in Fig. 8. (Compare with normal marrow of seven-day chick in Fig. 4.) ×800

which seemed to suffer relatively little from the radiation.

With regard to the problem of re-established hematopoiesis after radiation injury, it follows that, after radiation of the marrow has ceased, the injured hematopoietic tissue, composed mainly of a relatively unchanged reticulo-endothelial stroma and a few remaining hematopoietic cells, is still fertile ground for hematopoietic activity. This is evident from the resumed activity on the part of the residual

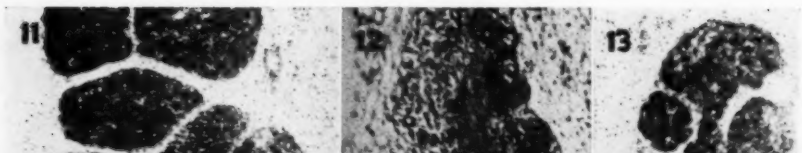


Fig. 11. Thymus from normal thirteen-day embryo. Note large lobules well filled with lymphocytes. The medulla can be seen near the bottom of the picture. ×100

Fig. 12. Thymus from thirteen-day embryo given 120 μc on fourth day of incubation. It is smaller, with fewer lymphocytes than normal. On the left, the fibroreticular stroma can be discerned, but it is almost devoid of lymphocytes. ×100

Fig. 13. Thymus from fifteen-day embryo given 180 μc on fourth day of incubation. It is much smaller than normal thirteen-day embryo thymus and does not show the usual cortical medullary division. ×100

hematopoietic cells. It is obvious that the marrow stimulants would be of very limited value in the almost complete absence of hematopoietic cells. Transfusion would be effective, but only temporarily; as a measure for a large number of cases, it is impractical. If feasible, the development of a method of replenishing the diminished marrow cells would afford a rational approach to the treatment of such injuries.

EFFECT OF RADIATION ON LYMPHOID TISSUE

The circulating lymphocytes arise largely in the thymus, spleen, cecum, and tonsils. Since lymphopoiesis is the same in all locations, we will limit our discussion to the thymus. The thymus consists of two paired chains of nodules extending through the whole length of the neck and lying adjacent to the carotid sheaths for most of their course.

About the twelfth day of incubation, when the blood islands of the yolk sac begin to degenerate and the bone marrow takes on the function of hematopoiesis, the primitive epithelial anlage of the thymus becomes lymphoid in character and shows much mitotic activity. This change in the character of the thymus appeared to be an *in situ* differentiation of the epithelial cells rather than a result of infiltration of lymphoid cells from the outside. From the twelfth to the sixteenth day, a high mitotic rate in the lymphocytes continues and the thymus attains its definitive structure. It is histologically very similar to human thymus—*i.e.*, a cortex densely packed with small and medium lymphocytes in an inconspicuous reticular stroma and a medulla composed of a reticulo-endothelial stroma in which are found Hassall's corpuscles and a thin scattering of lymphoid cells. The thymus retains this structure and continues to grow during the first two months of life.

The injection of 100 μc into fourteen-day-old embryos caused an almost immediate complete cessation of mitosis, followed in two to three weeks by excessive proliferation of lymphocytes. Suppression of mitosis was noted two to four days after injection, when there was an average of one mitosis per oil-immersion field as compared to twelve to fifteen mitoses in the normal thymus of the same age. At this time, the number of lymphocytes was obviously diminished and the bulk of the organ had decreased to three-fourths of its normal size. But five days after injection the mitotic counts were a third instead of a twelfth of the normal, and a day later, *i.e.*, six days after injection, mitoses had increased to half the normal,

although the loss of lymphocytes in the cortex was still evident (Fig. 16). A reactive over-compensation was apparent eighteen to twenty-two days after injection, when the mitotic count was four times higher than normal.

As would be expected, 200 μc on the fourteenth day of incubation produced a more severe and prolonged injury. A practically complete cessation of mitosis, together with destruction of many lymphocytes, occurred in two to four days as with the smaller dose, but the response to this injury was delayed and there was a lapse of four to six days rather than one to three days before mitosis returned to half the normal and the depleted structure began to fill in with immature lymphocytes. The response to injury, as evidenced by excessive mitotic division in the lymphoid cells, was similar to that noted with the smaller dose. Mitotic counts were five times the normal values, sixteen, eighteen, and twenty days after injection. By this time the thymus had recovered to virtually normal structure, but there were still agranulocytosis and a near-fatal anemia, and the bone marrow was only beginning to show regeneration.

The same sequence of changes was noted when 120 μc was administered to an embryo four days old. Nine days later the thymus was half the normal size, only partly filled with lymphocytes, and entirely devoid of mitoses (Fig. 12). Some evidence of recovery was noted three to five days later, on the eleventh and fourteenth days after injection, with a rise in the mitotic count to half the normal and a majority of large and immature lymphocytes. Histologically, recovery was complete nine days after the appearance of the most severe injury and eighteen days after injection. The thymus was still small, however, but in a seven-week-old bird there was no evidence that the gland had been injured.

A prolonged retardation of growth of the thymus was noted after injection of 180 μc on the fourth day of incubation. Nine days after injection the thymus was one-half normal size and closely resembled that of an embryo two or three days younger, except for decreased mitotic activity. Eleven days after injection, the thymus was still one-half normal size but showed a normal mitotic rate (Fig. 13). There seemed to be an inhibition of formation of the usual cortico-medullary structure. The thymus was composed mainly of a reticulo-endothelial stroma and large, immature lymphoid cells, with only a few mature lymphocytes. Seventeen days after injection, the cortico-medullary structure was present and mitotic activity was normal, but the thymus was two-thirds normal size. Two hundred μc on the eighth day of incubation had a more marked inhibitory action but the effect was otherwise similar. Twelve days later, the thymus was one-third normal size, the cortex was poorly developed, and little mitotic activity was present (Fig. 15). Twenty-seven days after injection, the then fifteen-day-old chicks were moribund from extreme anemia, but mitotic activity was at a normal level in the thymus, although the organ was still small and presented

Fig. 14. Thymus from normal nineteen-day embryo (one day before hatching). Note thick cortex well packed with lymphocytes. ×50

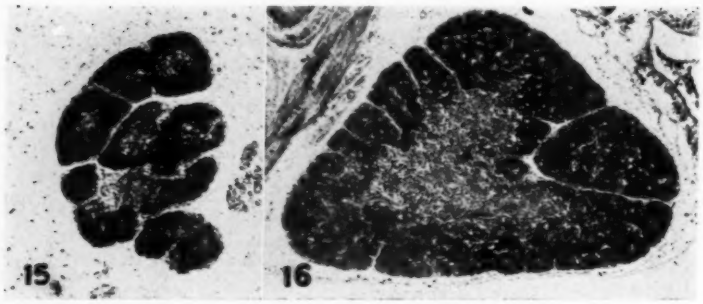


Fig. 15. Thymus from one-day chick given 200 μc on eighth day of incubation. It is markedly hypoplastic and shows no cortical medullary division. ×50
Fig. 16. Thymus from hatching chick given 100 μc on fourteenth day of incubation. It is smaller than control in Fig. 14, and its cortex shows loss of lymphocytes. ×50

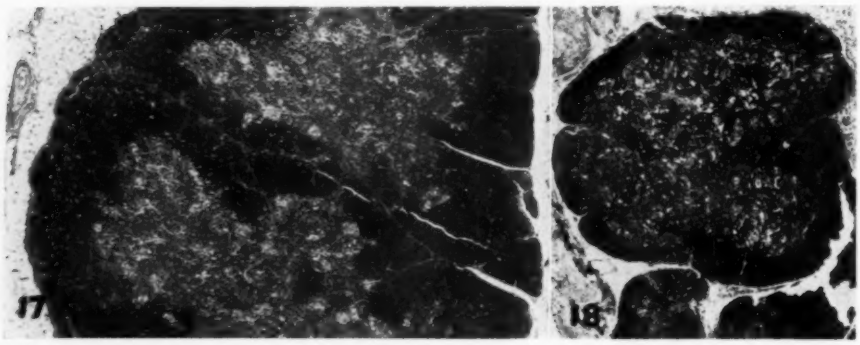


Fig. 17. Section through thymus of normal fifteen-day chick. Cortico-medullary structure is well formed and cortex is densely packed with lymphocytes. ×40
Fig. 18. Thymus from fifteen-day chick given 200 μc on eighth day of incubation. It is markedly hypoplastic. Cortex is poorly developed and in some places absent entirely. Because of the small size of the thymus, the Hassall's corpuscles are closer together than normal and give the impression of relative increase. ×40

numerous cortical hemorrhages (Fig. 18).

Injection of chicks produced an injury and recovery similar to that found in irradiated embryos, the injury being proportional to the amount of radiation. The fatal and near-fatal doses produce changes identical to those seen in the moribund fifteen-day chicks given 200 μc on the eighth day of incubation.

Discussion: In summarizing the effects on the lymphoid tissue in the thymus, there are several things that stand out. First, the high degree of sensitivity to radiation of the lymphocytes is shown by the marked suppression of mitotic activity and in appreciable thinning out of the cells two to four days after injection. This occurred even with the smallest dose of 100 μc. Only the gonads showed as early a response as this.

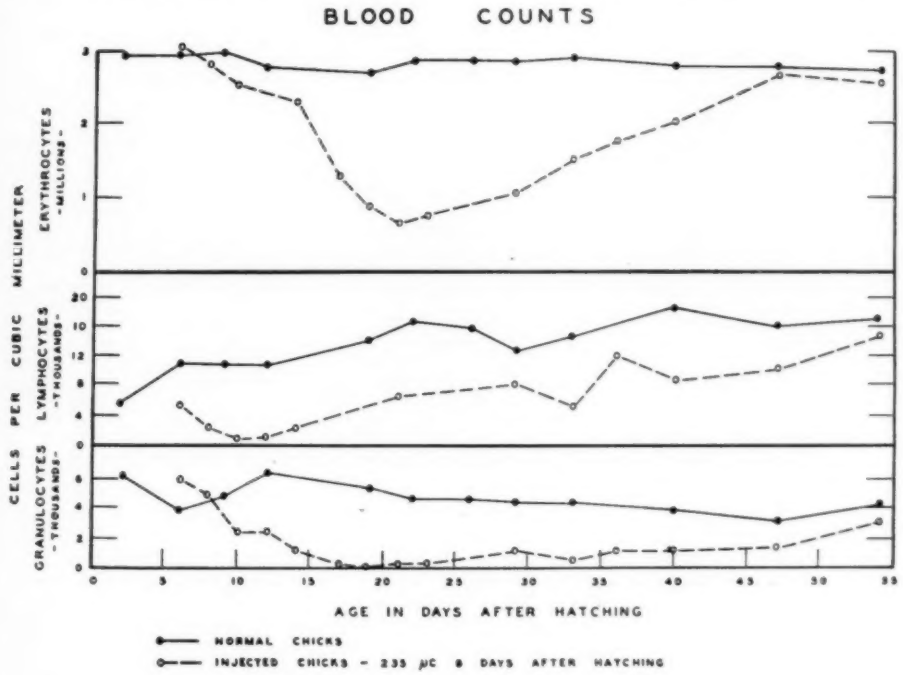
Second, regeneration of lymphoid tissue was rapid and started soon after injury. Except when large doses were given to young embryos, recovery was complete even in animals dying from anemia. Recovery was initiated from two to six days after the most severe depression of mitotic activity and was complete usually in less than three weeks. The histologic recovery of the thymus was more rapid than the recovery of the circulating lymphocyte count. The excellent recovery was no doubt due to the short duration of the injury. This was greatest during the

first few days after injection, before there was any appreciable concentration in the bone and the P^{32} was more or less uniformly distributed through the embryo.

Third, the response to the injury was not only prompt and adequate, but was excessive. Long after the thymus had returned to a normal histologic condition the mitotic activity remained abnormally high. This may be related to the compensating hyperplasia seen in some animal tissues following irradiation.

The averages of the blood counts of these groups of birds are given on Graphs I, II, and III as absolute counts of red cells, granulocytes, and lymphocytes per cubic millimeter. Values obtained from the control birds are also given on each graph.

Blood cells in circulation are relatively resistant to radiation (1). The course of blood counts during and after irradiation is largely determined, therefore, by two factors: first, the degree of injury to the immature and developing cells of the hemopoietic system, and second, the length of life of the circulating cells. The previously described changes in the bone marrow of irradiated embryos and chicks showed that there was no great difference in the radiosensitivity between the granulocyte series and erythrocyte series. The lymphoid tissues, on the other hand, showed earlier injury and more rapid recovery than did bone marrow, partly because of the concentration of P^{32} in the bones, which permitted only a relatively



Graph I.

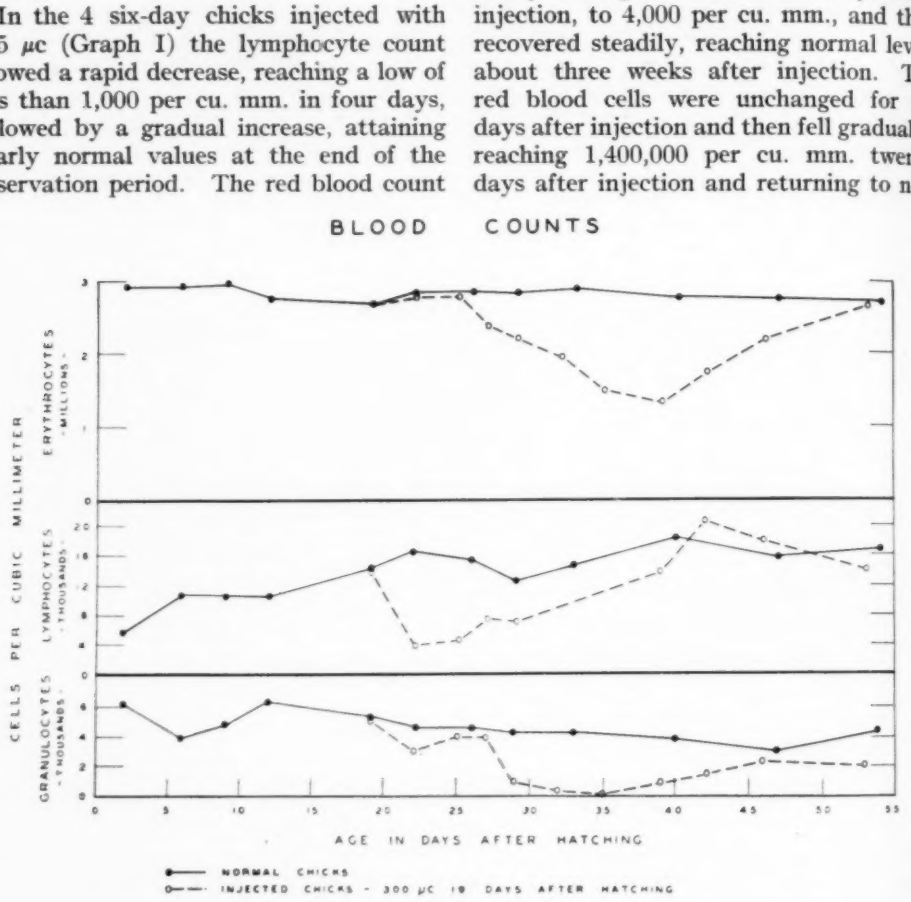
EFFECT OF RADIATION ON PERIPHERAL BLOOD COUNTS

To establish the changes in the peripheral blood counts during and following irradiation, we subcutaneously injected chicks of three different age groups with P^{32} and compared the blood counts with counts obtained from ten control chicks raised under the same conditions. Four six-day chicks were injected with 235 µc, 4 nineteen-day chicks with 300 µc, and 3 twenty-eight day chicks with 760 µc.

short period of irradiation of the lymphoid tissue. It would therefore be expected that lymphocyte counts would follow a different pattern than the myeloid elements.

In the 4 six-day chicks injected with 235 μc (Graph I) the lymphocyte count showed a rapid decrease, reaching a low of less than 1,000 per cu. mm. in four days, followed by a gradual increase, attaining nearly normal values at the end of the observation period. The red blood count fell gradually during the first eight days and then dropped sharply, reaching a low of 630,000 per cu. mm. fifteen days after injection and returning to normal in forty-one days. The granulocytes decreased rapidly during the first four days and then more gradually, completely disappearing from the blood in fifteen days. They recovered more slowly than other cell types and were only approaching normal values at the end of our observation period, forty-eight days after injection.

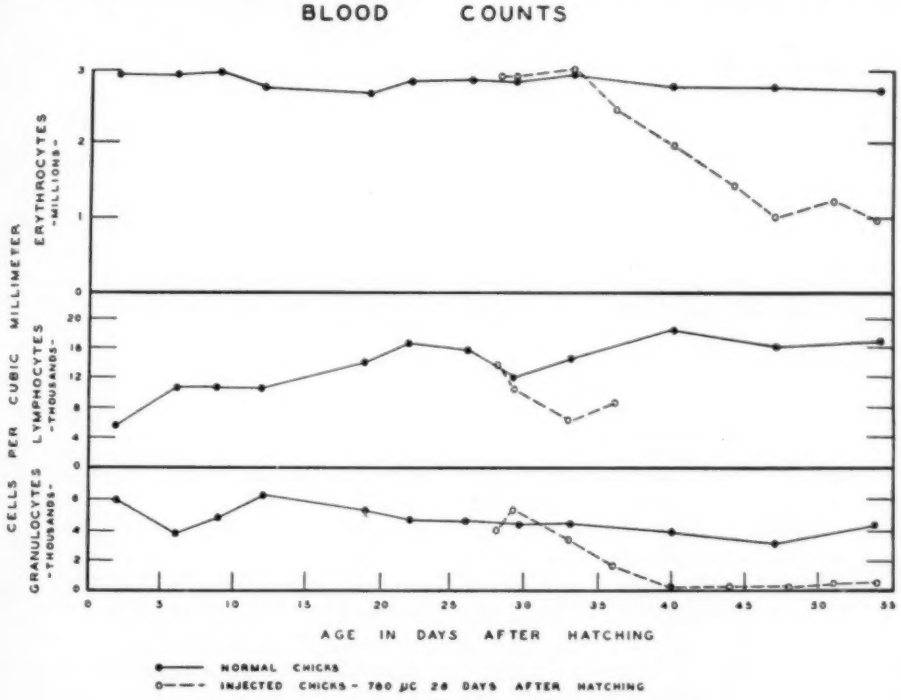
The blood counts of 4 nineteen-day chicks given 300 μc (Graph II) followed the pattern seen in the preceding group. The lymphocyte count dropped precipitously during the first three days after injection, to 4,000 per cu. mm., and then recovered steadily, reaching normal levels about three weeks after injection. The red blood cells were unchanged for six days after injection and then fell gradually, reaching 1,400,000 per cu. mm. twenty days after injection and returning to normal fourteen days later. The granulocyte count did not drop during the first week but then fell abruptly to 1,000 per cu. mm. ten days after injection. This count remained below 1,000 for ten days and then recovered, reaching near-normal limits at the end of the observation period, thirty-four days after injection.


BLOOD COUNTS
CELLS PER CUBIC MILLIMETER
ERYTHROCYTES - MILLIONS -
LYMPHOCYTES - THOUSANDS -
GRANULOCYTES - THOUSANDS -
AGE IN DAYS AFTER HATCHING
NORMAL CHICKS
INJECTED CHICKS - 300 μc 19 DAYS AFTER HATCHING

Graph II.

Our observation period did not extend to recovery of the 3 twenty-eight-day birds given 760 μc (Graph III). However, the same general pattern of early response

to radiation seen in the two preceding groups was repeated here. The lymphocyte count dropped sharply the first day and then more gradually, reaching a low of 6,000 per cu. mm. in five days before recovery began. No accurate lymphocyte counts could be calculated after the thirty-sixth day of age. The red count remained unchanged for five days and then fell off, reaching 1,000,000 per cu. mm. nineteen days after injection and staying near this level throughout the remaining week of observation. The granulocyte count rose slightly one day after injection and then fell gradually, these cells almost completely disappearing from the circulation twelve days after injection. This near-agranulocytic level was maintained throughout the remaining two weeks of observation.



Graph III.

Discussion: All groups showed the same general pattern of peripheral blood cell changes during and following irradiation. The lymphocyte count was affected first, falling sharply in the first few days and reaching a low point within three to five days after onset of radiation. The return to normal varied with the amount of radiation, and was shorter for lymphocytes than the other cell types, but was not as rapid as evidence of histologic repair in the thymus. The granulocytes dropped more gradually, and virtual agranulocytosis resulted in about two weeks. The recovery phase for the granulocytes was longer than for the other cell types. The red count remained within normal levels for several days and then gradually fell, reaching a low value in fifteen or twenty days. The recovery phase was only slightly longer than for the lymphocytes.

The lag period after irradiation before the fall of the red count is much longer in animals with non-nucleated red cells. Since the lag period is related to the length of life of circulating cells, it would appear likely that the circulating nucleated red blood cell in the chick is shorter-lived than non-nucleated red blood cells in mammals.

SUMMARY

Internal irradiation by P^{32} in smaller doses inhibited maturation of the immature hematopoietic cells and reduced the mitotic activity. These changes were reversible and after the radiation had diminished, the bone marrow returned to normal. The larger doses of radiation, which eventually caused a fatal anemia, produced an immediate and virtually complete cessation of mitotic activity and maturation. In this group, after the radiation had decreased significantly, the few remaining hematopoietic and reticuloendothelial cells began to show mitotic activity and maturation, but in an amount insufficient to prevent the development of an anemia which proved fatal several days later.

The lymphoid tissue of the thymus was very sensitive to radiation and showed an almost immediate marked reduction of mitotic activity, which lasted until most of the retained P^{32} had been concentrated in the bones. Recovery was rapid, and all but the most severe of these injuries were reversible.

Peripheral blood counts followed a definite pattern during and following irradiation. The lymphocyte count fell first and recovered before the other cell types. The granulocyte count fell next most rapidly and recovered most slowly. The red cell count dropped most slowly and returned to normal midway between lymphocyte and granulocyte counts.

NOTE: The authors are indebted to Dr. Olive Gates for invaluable assistance in this work.

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SUMARIO

Efectos de la Irradiación Continua sobre los Embriones de Pollo y los Pollos en Vías de Desarrollo. II. Médula Osea, Tejido Linfoideo y Sangre Periférica

Continuando sus estudios de los efectos de la irradiación continua, con P^{32}, sobre los embriones de pollo y los pollos en desarrollo, los AA. estudiaron la médula ósea, el tejido linfoideo y la sangre periférica.

Las dosis más pequeñas de irradiación interna con P^{32} inhibieron la maduración de las células hematopoyéticas inmaduras y atenuaron la actividad carioquinética. Esas alteraciones fueron reversibles, y después de disminuir la irradiación, la médula ósea volvió a lo normal. Las dosis mayores de rayos, que con el tiempo provocaron anemia letal, produjeron cese inmediato y virtualmente completo de la carioquinesis y la maduración. En este grupo, después de disminuir significativamente la irradiación, las pocas células hematopoyéticas y reticuloendoteliales restantes comenzaron a revelar actividad carioquinética y maduración, pero en proporción insuficiente para impedir la aparición de una anemia que resultó letal pocos días después.

El tejido linfoideo del timo se mostró muy sensible a la irradiación y reveló casi inmediatamente baja decidida de la carioquinesis que duró hasta que la mayor parte del P^{32} retenido se había concentrado en los huesos. La reposición fué rápida, y todas las lesiones, aparte de las más graves, fueron reversibles.

Las numeraciones de la sangre periférica se conformaron a un patrón bien definido durante la irradiación y después. La fórmula linfocitaria bajó y se repuso antes que las de las otras células. La fórmula granulocitaria vino después en la rapidez de su descenso y fué la que se repuso con mayor lentitud. La eritrocitaria fué la descendió más lentamente y en su retorno a lo normal ocupó un puesto medio entre la linfocitaria y la granulocitaria.

EDITORIAL

Fluoroscopy vs. Films in the Gastro-Intestinal Examination

The question of the relative values of fluoroscopy and radiography in the roentgen diagnosis of lesions of the gastro-intestinal tract has been perenially debated since the early days of roentgenology. In this country, Carman was a brilliant protagonist of the fluoroscopic examination, developing it to such a high degree that radiography, in his hands and those of his followers, assumed secondary importance. Cole and his associates, on the contrary, were strongly convinced that serial roentgenograms taken in several positions, to show all parts of the stomach, were the primary requisite for exact diagnosis. These opposing views have undergone many modifications with the passage of the years until today a standard gastro-intestinal study usually represents a skillful blending of the two.

Other factors have come to play a role from time to time, and each has left its imprint on the general picture. The danger to the operator inherent in fluoroscopy was early recognized, and even Carman (1), the foremost advocate of the method, warned of its attendant hazards, especially damage to the blood and blood-forming organs. The increasing incidence of diseases of the hemopoietic system among radiologists is ample proof that this warning was timely and—unfortunately—that it has been too largely disregarded. Spot-film radiography has slowly come into the picture and has found numerous advocates of various degrees of enthusiasm. Many have used it hesitantly because of the fear of roentgen injury either to the patient or to the operator. More recently photoroentgenography, with multiple exposures on small films, has entered the field, and its possibilities for supplanting the older methods of examination are being explored at several radiological centers.

In a Symposium presented at the 1948 meeting of the Radiological Society of North America, printed in the present issue of RADIOLOGY, the various aspects of this problem are discussed in the light of modern roentgenology. Harris furnishes a well rounded picture of the technic of fluoroscopy and the results which may be attained by its use. He holds it to be of prime importance in the diagnosis of lesions of the stomach and duodenal cap and regards films as of secondary significance. Templeton, while agreeing that fluoroscopy is an essential part of the examination, believes that films will often reveal lesions which the fluoroscopist has missed, and that the objective evidence which they furnish is of definite advantage. He advocates the use of the filming fluoroscope to obtain serial films of all parts of the stomach and amplifies the details of this technic in his discussion following the symposium. Morgan has contributed valuable information regarding the physical problems of fluoroscopy and spot-film radiography and offers practical suggestions for safeguarding both the patient and the radiologist—a matter which requires periodic reiteration. The excellent papers on gastroscopy, by Dailey, and on the clinical aspects of peptic ulcer, by Wilbur and Watts, round out the discussion and are deserving of careful study.

In reaching a decision as to the technic to be followed in examination of the gastro-intestinal tract, one must consider the ends to be accomplished. It goes without saying that the primary objective is an accurate diagnosis of the earliest manifestations of any organic lesion, more es-

pecially cancer. This granted, certain other considerations call for attention. In institutions where the emphasis is upon teaching, it is inevitable that films will play a prominent role, as the fluoroscopic image can be viewed by relatively few students. A similar condition will obtain in situations where the referring physician is accustomed personally to review the films. In clinics where routine gastro-intestinal studies are a common practice, the radiologist may decide upon the type of procedure which he feels will assure a high degree of accuracy without unduly prolonging the exposure time. It is thus apparent that no one type of examination can arbitrarily be designated the "best" for all radiologists or all institutions.

Where large numbers of gastro-intestinal studies are performed, with a considerable radiation exposure, it is acknowledged that there is a measurable risk involved. It is also pretty generally agreed that, under present conditions, in spite of this potential danger, fluoroscopy must occupy an important place in the examination. It behooves the radiologist, therefore, to see that his department is sufficiently staffed to permit a rotation of work, so that each fluoroscopist may regularly spend a certain number of days at duties not involving exposure to radiation. Nor can too strong emphasis be placed upon adequate protection in the form of lead rubber aprons and gloves, which are all too often omitted because of the inconvenience attending their use. The dangers of secondary radiation and how best to minimize them have been clearly pointed out by Morgan. Careful attention to these details will eliminate many of the hazards of fluoroscopy. Our younger men should be taught full respect for the dangers of radiation—as well as for its usefulness—and should be instructed as to the means of circumventing injury by observing simple rules of protection.

Technical changes are taking place that are modifying and may ultimately change completely our methods of gastro-intestinal examination. Already mass surveys are being made by Morgan (3) with the Schmidt camera. Others (2, 4) are conducting similar studies by fluoroscopy alone or in combination with films. The fluoroscopic method may itself be revolutionized, and its diagnostic efficiency multiplied, by further development of recently suggested procedures for amplification of the fluoroscopic image. With the clinical demands for mass surveys and the introduction of improved methods for their accomplishment, it is not beyond the realm of possibility that, like similar surveys in the field of tuberculosis, these may be used to screen out the normal subjects, while more complete examinations are reserved for those with evidence of an organic lesion.

REFERENCES

1. Carman, R. D., and Miller, A.: Occupational Hazards of the Radiologist, with Special Reference to Changes in the Blood. Radiology **3:** 408–417, November 1924.

2. Rigler, L. G.: Roentgen Examination of the Stomach in Symptomless Persons. J.A.M.A. **137:** 1501–1507, Aug. 21, 1948.

3. Roach, F., Sloan, R. D., and Morgan, R. H.: Detection of Gastric Carcinoma by Photofluorographic Methods. Am. J. Roentgenol. **61:** 183–187, 188–194, February 1949.

4. St. John, F. B., Swenson, P. C., and Harvey, H. D.: Experiment in Early Diagnosis of Gastric Carcinoma. Ann. Surg. **119:** 225–231, February 1944.

POSTGRADUATE COURSE IN MEDICAL ASPECTS OF NUCLEAR ENERGY UNIVERSITY OF CALIFORNIA

A postgraduate course in the medical aspects of nuclear energy is being offered at the University of California, San Francisco, Aug. 29 through Sept. 3, 1949. Dr. Joseph G. Hamilton, Associate Professor of Experimental Medicine and Radiology, University of California Medical School, and Associate Professor of Medical Physics and Director of the Crocker Laboratory, University of California, is General Chairman of the course. Other officers of instruction include, Luis W. Alvarez, Ph.D.; Austen M. Brues, M.D.; Simeon Cantril, M.D.; Andrew H. Dowdy, M.D.; John Gofman, Ph.D., M.D.; John H. Lawrence, M.D.; Bertram V. A. Low-Beer, M.D.; Edwin M. McMillan, Ph.D.; Stacy R. Mettier, M.D.; Earl R. Miller, M.D.; Edith H. Quimby, Sc.D.; Kenneth W. Scott, Ph.D.; Glenn T. Seaborg, Ph.D.; Curt Stern, Ph.D.; Robert S. Stone, M.D.; Robert L. Thornton, Ph.D.; Shields Warren, M.D.; Stafford Warren, M.D.

Inquiries as to enrollment should be addressed to Stacy R. Mettier, M.D., Office of Medical Extension, University of California Medical Center, San Francisco 22, Calif.

BROOKLYN ROENTGEN RAY SOCIETY

At a recent meeting of the Brooklyn Roentgen Ray Society, the following officers were elected for the ensuing year: President, Dr. John Pepe; Vice-President, Dr. B. Ehrenpreis; Secretary-Treasurer, Dr. J. Daversa, 603 Fourth Ave., Brooklyn, N. Y.

CHICAGO ROENTGEN SOCIETY

The newly elected officers of the Chicago Roentgen Society, for 1949–50, are T. J. Wachowski, M.D., President; Frank Hussey, M.D., Vice-President; John H. Gilmore, M. D., 720 N. Michigan Ave., Chicago 11, Secretary-Treasurer.

ARGENTINE RADIOLOGICAL ASSOCIATION

The newly organized Asociación Argentina de Radiología has announced plans for its Primer Congreso de Radiología to be held in Santiago del Estero, Argentina, in July 1949. The following are the official themes of the congress: Radiologic Exploration of the Bronchopulmonary System; Radiology of Bronchopulmonary Tumors; Radiology of Gastric Diseases; Radiology of the Extrahepatic Biliary Tract; Radiotherapy of Cutaneous Affections.

The President of the Association is Dr. Sabino Di Rienzo; Vice-President, Dr. Juan I. Zorrilla; General Secretary, Dr. Jose R. Aguirre; Permanent Secretary, Dr. Lidio G. Mosca, Tucuman 275, Santiago del Estero, Argentine; Treasurer, Dr. Robert Alvarez.

SUGGESTED MODEL CONTRACT FOR HOSPITAL RADIOLOGISTS

The attention of radiologists is called to a suggested model contract for hospital radiologists, appearing in *California Medicine* for April 1949. This contract was prepared by and as a result of joint conferences between legal counsel for the California Medical Association and counsel for the Association of California Hospitals. It has been approved by the Council of the Medical Association and at the time of publication was awaiting final action by a special committee of the hospital group.

DR. EDITH H. QUIMBY HONORED

Dr. Edith H. Quimby, Associate Professor of Radiology at the College of Physicians and Surgeons, Columbia University, was the recipient of one of the four American Design Awards for creative thinking annually presented by the firm of Lord & Taylor, New York City. The award, which was made at a luncheon at the Waldorf Astoria, on May 4, was in recognition of Dr. Quimby's work with radioactive materials.

BOOKS FOR CHILE

The National Committee for Chile is soliciting copies of medical periodicals of the last ten years and recent medical books for the library of the Medical School of the University of Chile, to replace reference material recently destroyed by fire. Any contributions should be sent to the National Committee for Chile, Room 318, Library of Congress, Washington, D. C.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE. A CLINICAL AND PHYSIOLOGICAL STUDY IN INFANTS AND CHILDREN. By ANDRÉ COURNAND, M.D., Associate Professor, Department of Medicine, College of Physicians and Surgeons, Columbia University, JANET S. BALDWIN, M.D., Assistant Professor, Department of

Pediatrics, New York University College of Medicine, and AARON HIMMELSTEIN, M.D., Instructor, Department of Surgery, College of Physicians and Surgeons, Columbia University. A volume of 108 pages, with numerous illustrations. Published by The Commonwealth Fund, New York, 1949. Price $4.00.

ATEMREGELUNG ALS HEILMITTEL. By Prof. Dr. LUDWIG HOFBAUER, Union University, Albany 3, N. Y. A volume of 100 pages, with 33 illustrations. Published by Wilhelm Maudrich, Wien, Austria, 1948. Price $2.50.

Book Reviews

LUNG DUST LESIONS (PNEUMOCONIOSIS) VERSUS TUBERCULOSIS. By LEWIS GREGORY COLE, M.D., F.R.C.R. A volume of 474 pages, with over 400 illustrations. Published by American Medical Films, Inc., White Plains, N. Y., 1948. Price $10.00.

In 1940, Lewis Gregory Cole, then Director of Silicotic Research for the John B. Pierce Foundation, and his son, the late William Gregory Cole, published their *Story of Dusty Lungs: A Preliminary Report.* There now appears this more elaborate treatise, summarizing the observations of these two investigators over a period of some fourteen years. They were assisted in their studies by many other workers in this field, to whom generous credit is given for case reports, specimens, and special forms of clinical and technical aid.

Dr. Cole states that his object has been to study the lungs of persons who have inhaled various quantities and qualities of dust and to present the results in simple terms with suitable illustrations, to describe the roentgen observations in such cases, and to correlate these with the pathological findings. He has sought further to distinguish dust lesions from those of other pathology and, finally, to apply the data which he has assembled to certain social and economic problems growing out of dust exposure in industry.

As the title indicates, particular stress is placed upon the similarity of many dust lesions to tuberculosis and the importance of comparing and differentiating the two, to which end a lavish use has been made of roentgenograms, photomicrographs, and drawings. The concluding chapter of the work is devoted to matters of technic, including details of the roentgenographic demonstration of chest lesions and a step-by-step description of the procedure employed for obtaining photomicrographs.

Dr. Cole's handling of his subject is original and stimulating, its very unorthodoxy contributing to its interest. Workers in this field will find this volume not only informative but thought-provoking to a high degree.

A SYMPOSIUM ON THE USE OF ISOTOPES IN BIOLOGY AND MEDICINE. Contributions by nineteen leading scientists. Report of a Conference conducted at the University of Wisconsin, Madison, Wis., September 1947. A volume of 446 pages. Published by the University of Wisconsin Press, Madison, Wis., 1948. Price $5.00.

There was held at the University of Wisconsin, in September 1947, a Symposium on isotopic research as applied to medicine and biology, participated in by the nation's leaders in this new field of study. The major papers of the Symposium are now published in book form, offering in the scope of a few hundred pages an authoritative exposition of this subject by those most highly qualified to discuss it.

An introductory chapter, furnishing an historical background for the use of isotopes in biochemistry, is followed by several papers on the preparation and availability of isotopes and their distribution by the Atomic Energy Commission; a group of technical articles on the preparation of compounds and measurements of radioactivity; a series on the results of tracer studies and their medical applications; a chapter on the therapeutic use of radioactive phosphorus and one on the treatment of thyroid disease by radioiodine. Two chapters are devoted to health hazards in the use of radioactive isotopes and measures for the protection of property and personnel. The concluding papers on the political and social implications of atomic energy sum up the attitude of the scientist to what is unquestionably the most serious problem of our time.

The number who had the privilege of attending the Symposium at Madison was limited. It is well to have made available to others who are interested in this new field of research the wealth of material that was presented there. This book is recommended as an authoritative and useful source of information to all who are engaged in research in the clinical application of isotopes to medicine and biology and to the far greater number who look with interest to the results of such investigations.

MEDICAL X-RAY PROTECTION UP TO TWO MILLION VOLTS. National Bureau of Standards Handbook 41, Issued March 30, 1949 (superseding Handbook 20). For sale by the Superintendent of Documents, Washington, D. C. Price 15 cents.

This handbook on roentgen protection was prepared by a Subcommittee made up of H. O. Wyckoff, *Chairman*, C. B. Braestrup, L. L. Call, E. E. Charlton, A. C. Cipollaro, M. D., M. Friedman, M. D., Russell Morgan, M.D., R. R. Newell, M.D., E. W. Philleo, Scott W. Smith, John Trump, and J. L. Weatherwax. It sets forth concisely standards of safety for the installation and use of high-voltage x-ray equipment. For further details of its preparation and content, see the Editorial by Dr. Lauriston Taylor in RADIOLOGY for May 1949.

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary*, Hugh F. Hare, M.D., 605 Commonwealth Ave., Boston 15, Mass.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary*, Harold Dabney Kerr, M.D., Iowa City, Iowa.

AMERICAN COLLEGE OF RADIOLOGY. *Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6, Ill.

SECTION ON RADIOLOGY, A. M. A. *Secretary*, U. V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. D. Anderson, M.D., 2501 6th St., Tuscaloosa.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary*, Sydney F. Thomas, M.D., Palo Alto Clinic, Palo Alto.

EAST BAY ROENTGEN SOCIETY. *Secretary*, Dan Tucker, 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary*, Wybren Hiemstra, 1414 S. Hope St. Meets monthly, second Wednesday, County Society Bldg.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB. *Secretary*, Charles E. Grayson, M.D., Medico-Dental Bldg., Sacramento 14. Meets at dinner last Monday of September, November, January, March, and May.

PACIFIC ROENTGEN SOCIETY. *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

SAN DIEGO ROENTGEN SOCIETY. *Secretary*, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

X-RAY STUDY CLUB OF SAN FRANCISCO. *Secretary*, Wm. F. Reynolds, M.D., University Hospital, San Francisco 22. Meets third Thursday at 7:45, January to June at Stanford University Hospital, July to December at San Francisco Hospital.

Colorado

COLORADO RADIOLOGICAL SOCIETY. *Secretary*, Mark S. Donovan, M.D., 306 Majestic Bldg., Denver 2. Meets third Friday of each month, at the Colorado School of Medicine and Hospitals.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, Fred Zaff, M.D., 135 Whitney Ave., New Haven. Meetings bimonthly, second Wednesday.

CONNECTICUT VALLEY RADIOLOGICAL SOCIETY. *Secretary*, Ellwood W. Godfrey, M.D., 1676 Boulevard, W. Hartford. Meets second Friday of October and April.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary*, Alfred A. J. Den, M.D., 1801 K St., N.W., Washington 6. Meets third Thursday, January, March, May, and October, at 8:00 P.M., in Medical Society Auditorium.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, F. K. Hurt, M.D., Riverside Hospital, Jacksonville. Meets in April and in November.

Georgia

ATLANTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Wm. W. Bryan, M.D., 490 Peachtree St., N. E. Meets second Friday, September to May.

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert Drane, M.D., De Renne Apartments, Savannah. Meets in November and at the annual meeting of State Medical Association.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary*, John H. Gilmore, M. D., 720 N. Michigan Ave., Chicago 11. Meets at the Palmer House, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly as announced.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, Harold L. Shinall, M.D., St. Joseph's Hospital, Bloomington.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, William M. Loehr, M.D., 712 Hume-Mansur Bldg., Indianapolis 4. Annual meeting in May.

Iowa

IOWA X-RAY CLUB. *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Anthony F. Rossitto, M.D., Wichita Hospital, Wichita. Meets annually with State Medical Society.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Everett L. Pirkey, M.D., 323 East Chestnut St., Louisville 2.

LOUISVILLE RADIOLOGICAL SOCIETY, *Secretary-Treasurer*, Everett L. Pirkey, Louisville General Hospital, Louisville 2. Meets second Friday of each month at Louisville General Hospital.

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday.

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary*, J. Howard Franz, M.D., 1127 St. Paul St., Baltimore 2.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary-Treasurer*, George Belanger, M.D., Harper Hospital, Detroit 1. Meetings first Thursday, October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, C. N. Borman, M.D., 802 Medical Arts Bldg., Minneapolis 2. Meets in Spring and Fall.

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, Wm. M. Kitchen, M.D., 1010 Rialto Building, Kansas City 6, Mo. Meetings last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Charles J. Nolan, M.D., 737 University Club Bldg. Meets on fourth Wednesday, October to May.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Ralph C. Moore, M.D., Nebraska Methodist Hospital, Omaha 3. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, George Levene, M.D., Massachusetts Memorial Hospitals, Boston. Meets monthly on third Friday at Boston Medical Library.

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary-Treasurer*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meetings quarterly in Concord.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Raphael Pomeranz, M.D., 31 Lincoln Park, Newark 2. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark.

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, J. Daversa, M.D., 603 Fourth Ave., Brooklyn. Meets fourth Tuesday of each month, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary-Treasurer*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meetings in January, May, and October.

LONG ISLAND RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening, October to May, at 8:45 P.M., in Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Wm. Snow, M.D., 941 Park Ave., New York 28.

QUEENS ROENTGEN RAY SOCIETY. *Secretary*, Jacob E. Goldstein, M.D., 88-29 163rd St., Jamaica 3. Meets fourth Monday of each month.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, Ralph E. Alexander, M.D., 101 Medical Arts Bldg., Rochester 7. Meets at Strong Memorial Hospital, third Monday, September through May.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary-Treasurer*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Charles Heilman, M.D., 1338 Second St., N., Fargo.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Carroll Dundon, M.D., 2065 Adelbert Road, Cleveland 6. Next meeting at annual meeting of the State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Paul D. Meyer, M.D., Grant Hospital, Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Seneca Hotel, Columbus.

CINCINNATI RADIOLOGICAL SOCIETY. *Secretary*, Eugene L. Saenger, M.D., 735 Doctors Bldg., Cincinnati 2. Meets last Monday, September to May.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John R. Hannan, M.D., Cleveland Clinic, Cleveland 6. Meetings at 6:30 P.M. on fourth Monday, October to April, inclusive.

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. E. Brown, M.D., 21st and Xanthus, Tulsa 4. Meets in October, January, and May.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Boyd Isenhart, M.D., 214 Medical-Dental Bldg., Portland 5. Meets monthly, on the second Wednesday, at 8:00 P.M., in the library of the University of Oregon Medical School.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4, Wash. Meets annually in May.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, Arthur Finkelstein, M.D., Graduate Hospital, Philadelphia. Meets first Thursday of each month at 8:00 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY. *Secretary-Treasurer*, R. P. Meader, M.D., 4002 Jenkins Arcade, Pittsburgh 22. Meets second Wednesday of each month at 6:30 P.M., October to June.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Maurice D. Frazer, M.D., Lincoln Clinic, Lincoln, Nebr. Next meeting in Denver, Colo., Aug. 18–20, 1949.

South Carolina

SOUTH CAROLINA X-RAY SOCIETY. *Secretary-Treasurer*, Robert B. Taft, M.D., 103 Rutledge Ave., Charleston 16.

South Dakota

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA. *Secretary-Treasurer* Marianne Wallis, M.D., 1200 E. Fifth Ave., Mitchell. Meets during Annual Session of State Medical Society.

Tennessee

MEMPHIS ROENTGEN CLUB. Meetings second Tuesday of each month at University Center.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Marsh Frére, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

Texas

DALLAS-FORT WORTH ROENTGEN STUDY CLUB. *Secretary*, X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meetings on third Monday of each month in Dallas in the odd months and in Fort Worth in the even months.

HOUSTON X-RAY CLUB. *Secretary*, Curtis H. Burge, M.D., 3020 San Jacinto, Houston 4. Meetings fourth Monday of each month.

TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth. Next meeting Feb. 3–4, 1950, in Dallas.

Utah

UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City. Meets third Wednesday, January, March, May, September, November.

Virginia

VIRGINIA RADIOLOGICAL SOCIETY. *Secretary*, P. B. Parsons, M.D., Norfolk General Hospital, Norfolk 7.

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Homer V. Hartzell, M.D., 310 Stimson Bldg., Seattle 1. Meetings fourth Monday, October through May, at College Club, Seattle.

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Theodore J. Pfeffer, M.D., 839 N. Marshall St., Milwaukee 2. Meets monthly on second Monday at the University Club.

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY. *Secretary*, S. R. Beatty, M.D., 185 Hazel St., Oshkosh. Two-day meeting in May; one-day with State Medical Society, September.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE. Meets first and third Thursdays 4 P.M., September to May, Service Memorial Institute, Madison 6.

Puerto Rico

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA. *Secretary*, Jesús Rivera Otero, M.D., Box 3542, Santurce, Puerto Rico.

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, E. M. Crawford, M.D. Associate Honorary Secretary-Treasurer, Jean Bouchard, M.D. *Central Office*, 1535 Sherbrooke St., West, Montreal 26, Quebec. Meetings in January and June.

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES. *General Secretary*, Origéne Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday each month.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA. Offices in Hospital Mercedes, Havana. Meets monthly.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA, *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, México, D. F. Meetings first Monday of each month.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Pathologic Non-Neoplastic Intracranial Calcification. John D. Camp. J. A. M. A. **137:** 1023–1030, July 17, 1948.

In this excellent summary the author has classified intracranial calcification of non-neoplastic origin as follows:

1. *Vascular lesions:* Arteriosclerosis, aneurysm, angiomatous malformations, and hematomas.
2. *Inflammatory lesions:* Previous encephalitis and tuberculosis.
3. *Parasitic disease:* Toxoplasmosis, cysticercosis, and trichinosis.
4. *Degenerative lesions:* Congenital or developmental in origin.
5. *Tuberous sclerosis.*
6. *Parathyroid insufficiency.*

Although the reproductions in the journal are, unfortunately, only fair, it is recommended that the reader consult the original article. PAUL W. ROMAN, M.D.
Baltimore, Md.

Atlanto-Epistropheic Luxation with Aplasia of the Dens Epistrophei. Kurt Nievergelt. Schweiz. med. Wchnschr. **78:** 653–657, July 10, 1948. (In German)

Four cases are reported in which hypoplasia or absence of the dens of the epistropheus, or its development as a separate ossicle, allowed forward luxation of the axis following trauma of varying severity. For treatment of this condition, the author prefers reduction under anesthesia and immobilization in plaster, followed at a later date by operative fusion of the upper cervical vertebrae to the skull.

Two roentgenograms; 2 photographs; 7 drawings.
LEWIS G. JACOBS, M.D.
Oakland, Calif.

THE CHEST

Tumors of the Breast: Preoperative Roentgenography. J. Gershon-Cohen and Philip J. Hodes. Surg., Gynec. & Obst. **86:** 723–728, June 1948.

The authors believe that roentgenographic examination of the breast, as well as of the lungs and skeleton, should be employed routinely in the preoperative study of breast tumors. Roentgenography of the breast itself is of greatest value in those cases where clinical examination and transillumination have failed, as in the large fatty breast with a small tumor and the rarer deep-lying breast mass protected from palpation by the overlying tissues. Occasionally, also, an additional lesion, not suspected on physical examination, is found. In most other instances, roentgenographic examination of the breast provides confirmation of a previously diagnosed tumor.

In experienced hands, the benign or malignant status of a tumor can often be judged, but in any questionable case, prompt biopsy is, of course, indicated. The roentgenogram can further aid the surgeon by delineating the pathological structure of the lesion, and it provides a record for comparison in those lesions that change in size from time to time.

The authors point out that the proper roentgen interpretation of breast tumors is extremely difficult, requiring excellent technic and considerable experience. An examination of both breasts and axillae should be included so that the metastatic, as well as the primary lesion, can be studied. The differential densities of the skin, subcutaneous fat, veins, lipoid tissue of the breast, glandular elements, and fascia of the suspensory ligaments, permit roentgenographic visualization of these structures. Infiltration and proliferation of large cell masses are thus identified by the changes in mammary architecture which they produce, and by their delineation within the surrounding lipoid structure.

The roentgenographic changes seen in other breast conditions than neoplasms are also outlined.

Twelve illustrations, including 4 roentgenograms.
D. B. NAGLE, M.D.
University of Pennsylvania

Differential Diagnosis of Pulmonary Lesions. Stanley B. Clark. New York State J. Med. **48:** 1587–1592, July 15, 1948.

This is a paper written by a roentgenologist as a guide for physicians in general practice, who most often are the first to encounter pulmonary lesions and who first have occasion to correlate clinical, pathologic, and roentgenologic data in attempting to arrive at a correct diagnosis. The pathologic and roentgenologic findings are presented with this in mind, and the lesions are grouped according to the underlying process. The main headings, with the subjects included under them, are as follows. *Destruction of Pulmonary Tissue:* lung abscess and gangrene of the lung, bronchiectasis, tuberculosis, and the pneumoconioses. *Consolidation of Pulmonary Alveoli:* lobar or pneumococcal pneumonia, passive congestion, and pulmonary infarction. *Changes in Intrathoracic Tension:* atelectasis and emphysema. *Lesions Primarily Interstitial in Location:* primary atypical pneumonia and Boeck's sarcoid. *Replacement of Normal Pulmonary Tissue by a Pathologic Process:* primary and metastatic lung tumors. *Alteration in Pleural Density:* pleural thickening and pleural tumors.

Shadows Resembling a Cavity in Laminagrams, due do a Shell Fragment in the Chest Wall. Roger Even and Guy Morin. J. franç. de méd. et chir. thoraciques **2:** 260–261, 1948. (In French)

On routine chest fluoroscopy in a young adult male, a suspicious left infraclavicular shadow was noted. Standard films were reported negative but laminagrams revealed a shell fragment in the right lateral chest wall at a depth of 4 cm. from the back which had not been detected in the routine film. As more anterior segments were obtained with the laminagraph, a rounded translucent shadow was observed anterior to the foreign body, increasing in size as one neared the chest wall. These ring shadows were judged to represent artefacts.

The authors state that highly opaque shadows in laminagraphic films produce images in other planes and that the image increases in size as the sections are taken progressively farther from the opacity. The configuration of the shadows depends on the type of apparatus used. In machines using a linear motion, the shadow is

linear and streaky, resembling the drooping foliage of a willow tree, while in machines using a circular motion the artefact is circular in shape. A warning is given to be on the alert for such a phenomenon in the case of highly opaque calcifications in the chest producing false shadows of cavities.

Two roentgenograms. E. M. SAVIGNAC, M.D.
Detroit, Mich.

Diagnosis and Treatment of Bronchiectasis. George E. Spencer and Edward M. Kent. Pennsylvania M. J. **51:** 1122–1127, July 1948.

Bronchiectasis is the second most common disease of the lungs, being surpassed in incidence only by tuberculosis. It frequently goes undiagnosed, the symptoms being attributed to chronic bronchitis or asthma. There are four types: ulcerative, stenotic, fibrotic, and dry hemorrhagic. The disease usually involves one of the lower lobes at first but advances to other lobes as it progresses.

By far the most important procedure for the diagnosis of bronchiectasis is bronchography. This is best done in the morning, with the patient fasting. After a preliminary gargle with 0.5 per cent pontocain solution, he is seated on a stool in the fluoroscopic room, the tongue is grasped with the fingers, and 1.0 per cent pontocain is allowed to drip onto the back of it, as the patient breathes quietly. Up to 10 c.c. of the anesthetic may be used. The iodized oil is then administered by dropping it on the back of the tongue while the patient "pants like a dog." He is instructed to lean to one side while the first 10 c.c. are administered and to the other for the remaining 10 c.c. This insures filling of the bronchi of the right middle and lower lobes, the lingula of the left upper lobe, and the left lower lobe. If the upper bronchi are to be filled, the opaque oil is introduced through an intratracheal catheter with the patient on the fluoroscopic table, the head of which is lowered 5 to 10 degrees.

Postero-anterior and oblique views are usually sufficient for diagnosis. If bronchiectasis is present, the filled cavities will be clearly demonstrated, resembling the branches of a dead tree or a bunch of grapes.

The most important medical measure is postural drainage, morning and night. In cases with disabling disease, surgery may be indicated. Penicillin has become a major factor in preparation for operation. Lobectomy may be performed with surprisingly little postoperative discomfort.

Four roentgenograms. JOSEPH T. DANZER, M.D.
Oil City, Penna.

Pathology of Reinfection. Some Sources of Diagnostic Errors. Walter Pagel and C. H. C. Toussaint. Am. Rev. Tuberc. **58:** 85–97, July 1948.

Reinfection is defined as a tuberculous infection occurring in a person in whom a previous primary infection is anatomically healed. The new lesion then will take the form of a focus at the site of entry of the tubercle bacilli, followed by a caseous focus in the regional lymph nodes. The term superinfection is used to designate a repeated infection from without in a person in whom primary infection has not healed completely. The fresh focus of infection will not be followed by caseation in the regional lymph nodes.

To illustrate the difficulties of recognizing these types of tuberculosis clinically and pathologically, the authors employ a series of short case histories. These cases, mostly with postmortem observations, include examples of endogenous infection of recent origin from an apparently obsolete primary lesion; persistence of the "soft state" for a long time in either or both constituents of a primary complex; cases of reinfection as defined above, and lesions simulating reinfection.

Six roentgenograms; 5 photographs.

L. W. PAUL, M.D.
University of Wisconsin

Non-Tuberculous Pulmonary Calcification. John A. Prior. Ohio State M. J. **44:** 700–703, July 1948.

The author conducted surveys, including chest roentgenograms and tuberculin and histoplasmin skin reactions, on a group of 5,087 Ohio State University freshmen and student nurses, all of whom were lifetime residents of some one county in Ohio. The southwestern segment of Ohio gave the highest incidence of histoplasmin positives, 75.8 per cent. The percentages tended to diminish in the neighboring areas, with the lowest incidence in the northeastern part of the state. Individuals coming from farm districts had a 9.5 per cent higher incidence of histoplasmin sensitivity than those coming from the cities. Sixteen per cent of those tested gave positive tuberculin reactions. Geographic differences were not apparent in this group, the incidence following the usual socio-economic pattern.

It is becoming increasingly apparent that not all parenchymal and hilar calcification is due to tuberculosis. A large percentage of such calcifications in individuals coming from the Southwestern States has been found to be due to *Coccidioides immitis*. Similarly, individuals coming from the Central Eastern States have parenchymal calcification due to histoplasmosis. Palmer (Pub. Health Rep. **61:** 425, 1946), who conducted a series of such tests, suggested that there may be a widespread benign form of histoplasmosis, as well as the more generally recognized fatal variety. Pulmonary calcification associated with positive histoplasmin reactions has been found to occur earlier in life than that in positive tuberculin reactors.

LOUIS BERNSTEIN, M.D.
Hartford, Conn.

Besnier-Boeck-Schaumann's Disease with Pseudo-Cystic Pulmonary Shadows. J. Brun and J. Viallier. J. franç. de méd. et chir. thoraciques **2:** 273–276, 1948. (In French)

A 39-year-old male gave a long history of functional and neurasthenic complaints—weakness, night sweats, paresthesias in the legs, severe frontal headaches, and a stubborn productive cough. At the age of 35, following a long drawn out febrile episode with cough and abundant sputum, a chest film was interpreted as showing evidence of tuberculosis. Despite prolonged care in and out of sanatoria, the functional disorders became more severe and frequent episodes of low-grade fever occurred, lasting two to three weeks, with shortness of breath, severe chest pain, and copious sputum.

When seen by the authors, the patient had been unable to work for two or three years. A series of roentgenograms extending over the past three years showed a bilateral widespread infiltration of the pulmonary parenchyma, quite dense and rather homogeneous in character, interspersed with clear polycyclic areas in the median third of both lungs. Lipiodol did not enter

these areas and there was no bronchial dilatation. The tuberculin test, sputum studies, sedimentation rate, and blood count were all normal. An epitrochlear node showed epithelioid cells surrounded by lymphocytes but no giant cells. Guinea-pig inoculations remained negative. The diagnosis was Besnier-Boeck-Schaumann's disease.

It is pointed out that nervous complaints so frequently precede or accompany this disease that they should be looked for in its evolution. The pseudocystic form of the disease has been reported very rarely. The authors believe it is the result of secondary emphysematous changes in the lung parenchyma following a pulmonary sclerosis by sarcoid tissue. The process is somewhat similar to the lung damage in silicosis. In the case reported, at least, the changes appear irreversible, with a poor prognosis for functional rehabilitation.

One roentgenogram. E. M. SAVIGNAC, M.D.
Detroit, Mich.

Besnier-Boeck-Schaumann's Disease with Multiple Localizations and with Involvement of the Myocardium and of the Endocardium. P. Bonnet and J. Brun. J. franç. de méd. et chir. thoraciques **2:** 276–280, 1948. (In French)

The case reported here is that of a 17-year-old girl who has been followed for four years. Her disease apparently evolved in two successive stages. At first there was a syndrome of uveoparotitis with paralysis of the 7th and 9th cranial nerves, a polyneuritis of the lower extremities, and enlargement of the mediastinal nodes. After a considerable improvement there then developed a miliary type of pulmonary spread and cardiovascular involvement, with splenomegaly and enlargement of the axillary lymph nodes. There were only transient cutaneous manifestations of an erythema nodosum type followed by an erythematous macular rash on the legs. Roentgenograms of the bones showed no changes.

The cardiac lesions were manifested clinically and radiologically by enlargement of the heart, chiefly of the left ventricle. A systolic mumur with transmission to the axilla developed, along with a palpable thrill. The consulting cardiologist believed that a true mitral stenosis had developed, with involvement of the endocardium by sarcoidosis. To date the literature has not mentioned endocardial sarcoidosis. Full proof is, of course, not available in this instance, but in the absence of any clinically recognizable rheumatic fever, it was believed by all the consultants that the evidence was in favor of endocardial and myocardial sarcoidosis.

Two roentgenograms. E. M. SAVIGNAC, M.D.
Detroit, Mich.

Sarcoidosis Following Primary Tuberculosis. A Case Report. Joseph S. Hiatt, Jr. Am. Rev. Tuberc. **58:** 98–101, July 1948.

A case is reported of pulmonary sarcoidosis developing in a 10-year-old Negro girl who was under observation for primary tuberculosis. Roentgenograms of the chest previously had shown a partially calcified primary complex and the tuberculin test was positive. During a follow-up examination approximately two and a half years later a considerable change was noted in the chest. There were linear and nodular densities throughout the lung fields and markedly enlarged mediastinal nodes. The previous primary complex remained unchanged. Biopsy of an enlarged epitrochlear lymph node revealed the changes of Boeck's sarcoid. The chest lesions and enlarged peripheral nodes improved and six months later had largely disappeared.

Four roentgenograms. L. W. PAUL, M.D.
University of Wisconsin

Metastatic Pulmonary Cancer Secondary to a Symptomless Cancer of the Pancreas. R. Benda, F. Franchel, and B. Duperrat. J. franç. de méd. et chir. thoraciques **2:** 268–272, 1948. (In French)

A 62-year-old woman suffering from chest pain, dyspnea, and a non-productive cough showed, on radiographic study of the chest, numerous closely packed, rounded opaque nodules measuring from 0.5 to 1.5 cm. in diameter, widely disseminated throughout both lungs. A thorough examination, including intensive radiographic and laboratory studies, failed to reveal the origin of these. It is particularly mentioned that there was no evidence of pancreatic disease.

At autopsy, the pancreas, though normal in size, was found on sectioning to be considerably hardened. Microscopic sections showed an extensive adenocarcinoma with a somewhat peculiar metastatic spread along the course of the nerve fibers. The lung sections showed metastatic adenocarcinoma. No other metastases were discovered.

The authors comment upon the frequently atypical clinical course of cancer of the pancreas. Only two cases showing metastases to the lungs were discovered in the French literature during the past fifteen years.

One roentgenogram; two photomicrographs.
E. M. SAVIGNAC, M.D.
Detroit, Mich.

Endobronchial Metastases with Symptomatology of Primary Bronchogenic Cancer. Roger Even and Jacques Lecoeur. J. franç. de méd. et chir. thoraciques **2:** 147–151, 1948. (In French)

Three cases of metastatic cancer of the bronchi are reported. The primary lesion was in the rectum in 2 cases and in the uterus in 1 case. One of the patients had metastatic lesions also in the lung parenchyma, but in the other two the clinical manifestations were those of bronchial obstruction and the tumors could be differentiated from primary bronchogenic carcinoma only by histologic means.

There are two types of bronchial metastases: in one, metastasis is directly to the bronchial wall; in the other, metastatic tumors in the lung parenchyma invade the bronchi secondarily. It is further suggested that certain opacities which are said to represent metastatic tumors *per se* are, in reality, areas of pulmonary infarction, the result of cancer-cell emboli.

The authors stress the importance of a careful systematic investigation in all cases of bronchial obstruction in order to determine whether the cause is a primary neoplasm or a metastatic tumor.

Nine roentgenograms; 2 photomicrographs.
RODERICK L. TONDREAU, M.D.
The Mayo Foundation

Secondary Bronchial Cancer with Symptomatology of Primary Bronchial Cancer. Lopo de Carvalho, J. M. Lemoine and Y. Rose. J. franç. de méd. et chir. thoraciques **2:** 156–160, 1948. (In French)

Seven cases of metastasis to the bronchi are reported.

Primary lesions were in the breast (5 cases), uterus (1 case), and testis (1 case). Diagnosis in such cases is not always simple. In certain tracheo-esophageal lesions, it is very difficult to determine the point of origin, since both structures have a common embryologic origin. The fact that a secondary tumor has the histologic characteristics of a primary tumor does not necessarily mean that the second tumor represents metastasis, for multiple primary lesions may exist.

The authors state that, in the face of bronchial obstruction, metastasis should be especially suspected (1) if the patient is a woman, because of the low incidence of primary bronchogenic carcinoma in females, and (2) in all cases in which biopsy reveals adenocarcinoma.

Six roentgenograms; 2 photomicrographs.

RODERICK L. TONDREAU, M.D.
The Mayo Foundation

The Pendulum Movement of the Mediastinum in Pneumothorax. Lopo de Carvalho, Aires de Sousa, and Carlos Vidal. J. franç. de méd. et chir. thoraciques 2: 245–251, 1948. (In French)

Because of contradictory statements in the literature regarding the direction of pendulum movements of the mediastinum in the presence of a pneumothorax, the authors have studied the problem with a special kymograph. This instrument features both horizontal and vertical slits which move simultaneously at right angles to each other, and, when used on the chest, permits a simultaneous study of rib and diaphragm motion on the one hand, and of mediastinal motion on the other.

It was found that invariably the mediastinum moves toward the collapsed lung during inspiration and toward the healthy side during expiration. This phenomenon occurred even in the presence of tension pneumothorax with greatly increased intrathoracic pressure. The only exception was in cases of viscero-parietal pleural adhesions or other lesions producing fixation of the intrathoracic structures.

The mediastinal motion is explained by the altered dynamics in pneumothorax. The increased negative pressure on the collapsed side during inspiration draws the mediastinum over, while on the healthy side the negative pressure increase is neutralized by the entrance of inspired air into the lung.

Five roentgenograms; one drawing.

E. M. SAVIGNAC, M.D.
Detroit, Mich.

Dermoid Cysts and Teratomas of the Mediastinum with Unusual Features. Herbert C. Maier. Arch. Surg. 57: 154–161, July 1948.

The author reports four cases because of the unusual features of the tumors found. In the first, a dermoid cyst of the mediastinum extended from the hilus into the left upper lobe, which was largely replaced by tumor. In the second, a teratoma of the mediastinum was discovered in a child of four years and successfully removed. In the third, two independent dermoid cysts were present, one projecting on either side of the mediastinum. Both were removed, but at two operations. In the fourth case a dermoid cyst with calcification in the walls was not seen to grow over a four-year period; nevertheless, at operation an infiltrating inoperable tumor was found, and the patient subsequently died of metastases.

Eleven roentgenograms. LEWIS G. JACOBS, M.D.
Oakland, Calif.

Incomplete Division of the Atrioventricular Canal with Patent Interatrial Foramen Primum (Persistent Common Atrioventricular Ostium). Report of Five Cases and Review of the Literature. H. Milton Rogers and Jesse E. Edwards. Am. Heart J. 36: 28–54, July 1948.

The authors report 5 cases of their own and give the essential pathological and clinical features in an additional 50 cases, reported in the literature, of the congenital anomaly characterized by incomplete division of the auriculoventricular canal. In 3 of the authors' cases the essential anomalies were virtually identical, consisting of a defect in the lower portion of the interauricular septum, a defect in the superior and posterior portion of the interventricular septum, and a single auriculo-ventricular canal guarded by one valve, which was common to both sides. The essential anomalies in the other 2 cases were a defect in the lower portion of the interauricular septum and a cleft in the anterior or aortic cusp of the mitral valve. The tissue of the aortic cusp of the mitral valve and that of the septal cusp of the tricuspid valve were continuous beneath the defect in the interauricular septum. In one of these latter cases there was a second interatrial septal defect representing a widely patent foramen ovale.

In more than half of the 55 cases death occurred before the age of one year. Only 5 patients lived beyond thirty years. The lesion acts as a simple interauricular septal defect. Secondary changes are right heart enlargement and widening of the pulmonary artery orifice. Cyanosis may be present at birth, but is usually acquired. Cardiac murmurs are frequently observed.

A description of the development of the cardiac anomalies is included. Data for the 55 cases are tabulated, and references are appended.

Seventeen illustrations, including 3 roentgenograms; 2 tables.

HENRY K. TAYLOR, M.D.
New York, N. Y.

THE DIGESTIVE SYSTEM

Relaxation of the Gastric Mucosa Producing Pyloric Obstruction. Alfred Zacho. Arch. Surg. 57: 45–50, July 1948.

The presence of abnormally lax, redundant, and loosely attached mucous membrane in the pyloric region of the stomach may lead to obstructive symptoms, either as a result of actual prolapse through the pylorus or by the formation of a valve-like fold over the pyloric orifice. A case of each type is reported, with operative findings. Clinically the patients had increasing attacks of severe cramping epigastric pain, sometimes relieved by vomiting, and loss of weight. The roentgen findings in both cases suggested the presence of a tumor. Resection of the pyloric portion of the stomach led to a cure, and the resected specimens showed the marked laxness of the mucosa without other lesion.

One roentgenogram; 2 photographs.

LEWIS G. JACOBS, M.D.
Oakland, Calif.

Diverticula of the Stomach; Report of 26 New Cases. S. P. Bralow and M. A. Spellberg. Gastroenterology 11: 59–82, July 1948.

The authors review the literature and present a study of 26 additional cases of true diverticula of the stomach

and 4 cases of false or acquired diverticula. The reported incidence of gastric diverticula is from 0.02 to 2.6 per cent. There is a broad peak age incidence at thirty to fifty years. The posterior wall of the lesser curvature is the most common location. The range in size is considerable. The sac may contract after surgery so that it is much smaller than it appears, when distended by barium, on the roentgenogram. In one of the authors' cases the surgical specimen measured 7 × 4 cm., though roentgenographically the diverticulum was so large as to be mistaken for a cascade stomach.

The signs and symptoms are not characteristic and diagnosis is usually made by roentgenography or gastroscopy. The radiologic diagnosis is based on retention of the opaque medium in the diverticular sac after the remainder of the stomach has emptied. The diagnostic requirements as laid down by other writers are: (1) a mobile sac not attached to extragastric tissues; (2) a well defined, smooth shadow observed from various angles; (3) generally absence of tenderness; (4) demonstration of rugae in the mucosal lining of the neck; (5) location on the lesser curvature of the posterior wall of the cardia; (6) in some cases ability to empty the sac by change of position.

Gastroscopy is of especial importance for ruling out other conditions, as gastric ulcer, since the appearance is quite characteristic. In 2 cases seen by the authors a lesion diagnosed radiologically as a diverticulum was shown gastroscopically actually to be an ulcer. In one case with negative roentgenograms, gastroscopy revealed a diverticular ostium, but in 2 instances a diverticulum demonstrated radiologically was missed, probably because of its location.

Associated gastro-intestinal disease is frequent, and the mere presence of a diverticulum should not be accepted as the sole factor responsible for symptoms. On the other hand, the condition may produce pain, vomiting, and hemorrhage of incapacitating character.

Thirteen illustrations, including 10 roentgenograms.

J. D. CALHOUN, M.D.
University of Arkansas

Cavernous Angioma of the Stomach. Rosario Impallomeni and Aldo Greco. Radiol. med. (Milan) **34:** 343–348, June 1948. (In Italian)

The authors describe a case of cavernous angioma (proved at operation) involving the upper portion of the greater curvature of the stomach. The radiologic appearance was that of a flat filling defect without obliteration of the mucosal folds. The clinical complaint was pain following meals. No gross or occult blood was found.

Three roentgenograms.

CESARE GIANTURCO, M.D.
Urbana, Ill.

Leiomyosarcoma of the Stomach: Review of Sixteen Cases and a Report of a Case of Multiple Leiomyosarcomas of the Stomach. Charles P. Marvin and Waltman Walters. Arch. Surg. **57:** 62–70, July 1948.

Leiomyosarcoma is the rarest of the gastric sarcomas, constituting about 10 per cent of the total. The records of the Mayo Clinic from 1907 through 1946 contained 16 cases; during the same period 10,000 surgically verified cases of gastric carcinoma were seen. The tumor has no sex predilection and may occur at any age, the average being about forty-five years. Symptoms are not specific and often resemble the ulcer syndrome. The most characteristic syndrome is hemorrhage, pain in the left upper quadrant or epigastrium, and an upper abdominal mass. Achlorhydria was present in 3 of the 11 patients subjected to gastric analysis. The roentgen picture is also not characteristic, often leading to a diagnosis of carcinoma. Schindler and his co-authors believed a gastric filling defect with a central niche and fistulas to be suggestive of the diagnosis, but this was not true of the series of cases here studied, only 1 of which showed this triad on dissection.

The tumors varied from Grade I to Grade III (Broders); in only two were the adjacent nodes involved. Distribution in the stomach was random, all portions being affected. Ulceration was present in 8 cases.

Treatment is surgical. Ten of the authors' patients had subtotal gastrectomy, 1 had total gastrectomy, and 5 had transgastric local excision. Of 15 patients traced, 6 are alive for periods varying from three months to seven years; 2 died postoperatively, and 7 died at various periods up to four years. The prognosis seems a little more favorable than in gastric carcinoma.

In a detailed case report on one of these patients, the authors describe the presence of multiple and apparently independent leiomyosarcomas.

Two tables.

LEWIS G. JACOBS, M.D.
Oakland, Calif.

A Study on the Occurrence of Pneumoperitoneum after Gastroscopy and the Observance of Interstitial Emphysema of the Stomach. James Myhre and J. Allen Wilson. Gastroenterology **11:** 115–119, July 1948.

Having found in the literature 13 cases of pneumoperitoneum following gastroscopy, the authors made a study of 119 consecutive gastroscopic examinees, with this eventuality in mind. In each instance an upright x-ray film of the abdomen was made twenty-four hours after the procedure. In none of these was a pneumoperitoneum found, but in 2 cases the roentgenogram showed a thin line of decreased density, presumably air, in the left upper quadrant of the abdomen closely approximating but separate from the air bubble in the stomach. This was diagnosed as interstitial emphysema of the stomach. The second case was followed serially and the density disappeared in seventy-two hours. Both patients were asymptomatic.

Previous reports comment on the lack of evidence to suggest perforation of the stomach wall by the gastroscope. The authors feel that a perforation is probably not necessary but that interstitial emphysema is one of the steps in progression to gross leakage into the peritoneal cavity.

Three roentgenograms.

[In this same issue of Gastroenterology (pp. 127–129) there appears a report, by Lichstein and Wharton, of a case of pneumoperitoneum following gastroscopy in which no perforation could be found at laparotomy three hours later.—ED.]

GEORGE REGNIER, M.D.
University of Arkansas

Multiple Duplicative Cysts of the Duodenum Causing Acute Intestinal Obstruction in a Girl Five and One-Half Years of Age. N. Frederick Hicken, Vernon L. Stevenson, John H. Carlquist, and Q. B. Coray. Am. J. Surg. **76:** 92–98, July 1948.

The authors report the occurrence of two duplicative

cysts of the duodenum, producing a compressive obstruction of the descending and transverse segments, in a child of five and a half years.

Congenital duplications may occur in any portion of the alimentary tract. If the mucosal component becomes active, the retained secretions may produce a cystic tumefaction which by extrinsic pressure obstructs the parent structure. The duodenum is seldom affected by these congenital duplications, only 9 cases appearing in the literature. None of these was recognized before surgical intervention or postmortem examination. The authors' case was considered on roentgen examination to be one of retroperitoneal tumors. Only at operation was its true nature recognized.

The authors make the point that roentgenologic studies afford the only method of making an accurate preoperative diagnosis. The scout films usually localize the obstruction in the duodenum by outlining the distended, gas-filled stomach, while the small intestines and colon harbor but little gas. Peristaltic waves are seen to originate in the stomach and end abruptly at the obstruction. Fluoroscopy is particularly informative, as the ingested barium can be seen to traverse the attenuated but displaced duodenum. As the cyst lies in the gastroduodenal ligament, it pushes the duodenum upward and outward, thereby widening the U-shaped appearance of the duodenal loop. The fact that the tumor is periduodenal immediately precludes the possiblity of a hypertrophied pyloric ring. Duodenal diverticula may occupy the same position but always communicate with the intestinal lumen and hence become filled with the contrast medium. Partial atresia results in a narrowed duodenal lumen which occupies a normal anatomic position and is not rotated, compressed, or dislocated by adjacent tumefactions.

Remedial surgery affords the only opportunity for survival. Some cases may be suitable for local resection, but in the majority a posterior gastrojejunostomy must be done in addition.

Four illustrations, including 2 roentgenograms; 1 table.

MARLYN W. MILLER, M.D.
University of Pennsylvania

Gallstone Ileus Associated with Diverticulitis of the Colon. A Case Report. Irving I. Lomhoff and Jerome Dubowy. Am. J. Roentgenol. **60:** 86–89, July 1948.

The authors present a case of gallstone ileus with an associated diverticulitis. The 71-year-old patient was treated conservatively and recovered. She was dismissed from the hospital with the diagnosis of intestinal obstruction due to diverticulitis and passed the large gallstone at home. In retrospect the gallstone was identified in the barium enema study.

The incidence of gallstone ileus is low (0.4 to 5.0 per cent of all intestinal obstruction). Its importance lies in its high mortality, about 50 per cent. In the large majority of cases the stone becomes lodged in the small intestine. In a series of 125 cases reported by Foss and Summers (Ann. Surg. **115:** 721, 1942. Abst. in Radiology **39:** 751, 1942), only 3.3 per cent involved the large bowel.

The importance of considering gallstone impaction in the differential diagnosis of intestinal obstruction is stressed, especially if one is dealing with elderly females with a history of gallbladder disease.

Five roentgenograms.

JAMES C. KATTERJOHN, M.D.
Indianapolis, Ind.

Chronic Relapsing Pancreatitis: An Analysis of 27 Cases Associated with Disease of the Biliary Tract. Earl E. Gambill, Manfred W. Comfort, and Archie H. Baggenstoss. Gastroenterology **11:** 1–33, July 1948.

Chronic relapsing pancreatitis typically manifests itself by recurring attacks of pain in the upper part of the abdomen, by disturbances of function of acinar and islet cells, and by certain sequelae. It is a distinct clinical entity and does not require the presence of disease of the biliary or gastro-intestinal tract for its inception or continuation. Biliary tract disease is present, however, in many cases.

The authors present an analysis of 27 cases of the condition associated with biliary tract disease encountered in the Mayo Clinic in the years 1939–43, and compare their findings with those in a series of 29 cases without associated biliary tract involvement done during the same period.

Several interesting observations are made. In the group with associated biliary tract disease about 25 per cent of the patients gave a history of heavy use of alcohol. An acute and painful seizure usually marked the onset of the disease and was the most violent manifestation, but the character of the pain varied. Pain frequency and severity usually increased. About 10 per cent of the patients had glycosuria. In only 3 of the 10 cases in which the fasting concentration of blood sugar was determined was it greater than 120 mg. per 100 c.c. A preoperative diagnosis of chronic pancreatitis was infrequent.

Cholecystography was done in only 3 of the 10 cases in which the gallbladder was present at the time of examination. Gallbladder function was shown to be normal in one, poor in a second, and absent in the third. A roentgenogram of the gallbladder region, made in 6 cases, showed pancreatic calculi in 1. Films of the pancreatic region, made in 7 cases, disclosed calcification in 5. In order to exclude a renal origin for the painful seizures, excretory urography was done and served to reveal pancreatic calcification in 1 instance. Roentgenograms of the colon were normal in 5 cases, excluding it as the source of the trouble.

The clinical picture of the disease is apparently fairly constant regardless of the presence or absence of disease of the biliary tract, but the superimposition of the latter adds to the diagnostic problems. Correct diagnosis depends upon a high index of suspicion, roentgenologic findings, and pancreatic function tests.

Evidence is cited supporting the thesis that in chronic relapsing pancreatitis, disease of the biliary tract may be secondary to the pancreatic disease.

Nine photomicrographs.

J. D. CALHOUN, M.D.
University of Arkansas

THE MUSCULOSKELETAL SYSTEM

Eosinophilic Granuloma of Bone. Report of Six Cases. Joseph L. Platt and Richard B. Eisenberg. J. Bone & Joint Surg. **30A:** 761–768, July 1948.

This is a report of five cases in outline and one in detail of eosinophilic granuloma of bone. The patient whose history is given in detail was a white male, 14 years of age, who in January 1945 showed small irregular and confluent cystic areas in the neck and intertrochanteric region of the right femur. There was slight cortical thickening, suggesting periosteal reaction. Four months later, scattered osteolytic areas were seen in the left frontal bone, and one year later,

the lesion in the right femur showed considerable regression. A year and four months after first observation, a similar lesion developed in the right mandible at the angle. A biopsy showed eosinophilic granuloma. Irradiation therapy was administered to the various lesions, with prompt regression. One of the other cases also showed a similar response to irradiation therapy. Since these lesions are known to regress spontaneously, however, no definite claim for complete dependence on irradiation is made.

Eleven illustrations including 7 roentgenograms; 1 table.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Eosinophilic Granuloma of Bone with Diffuse Pulmonary Involvement. Douglas D. Dickson. California Med. **69:** 51–53, July 1948.

A case of eosinophilic granuloma of bone is reported with lesions involving the acromion, sacrum, ischium, greater trochanter, and vertebrae. Associated with these there was a diffuse nodular infiltration of both lung fields demonstrable roentgenographically. Bone biopsy revealed eosinophilic granuloma. X-ray therapy to the bone lesions produced a definite improvment, but the pulmonary lesions showed no response.

Four roentgenograms; 1 photomicrograph.

MAURICE D. SACHS, M.D.
Cleveland, Ohio

Solitary (Unicameral) Bone Cyst. Arthur G. James, Bradley L. Coley, and Norman L. Higinbotham. Arch. Surg. **57:** 137–147, July 1948.

This report deals with 26 cases of solitary bone cyst seen in the period 1933–46, and comparison is made with a group of the same number of cases seen from 1920 to 1933. This lesion is relatively rare, occurring in childhood and adolescence in the proximal ends of long bones, especially the humerus and femur. Physical findings are meager and non-specific; the roentgenogram shows a solitary area of bone destruction on the diaphyseal side of the epiphyseal line, circumscribed and surrounded by the expanded and attenuated cortex. Fine trabeculae often traverse the area; they are caused by ridges on the cyst wall. Several theories have been advanced as to the cause of these cysts, but none is entirely satisfactory.

Treatment is surgical. In 11 cases of the present series a simple curettage was done, and in 14 curettage plus bone transplantation. One patient was not treated. Four recurrences, 2 single and 2 repeated, were treated by reoperation; 1 required resection and segmental graft. Cavities are filled in with bone chips from the tibia or iliac crest. Radiation therapy is not recommended because of the unavoidable exposure of the epiphyseal plate, leading to growth disturbances. No example of sarcomatous degeneration was seen following surgery.

Six roentgenograms.

LEWIS G. JACOBS, M.D.
Oakland, Calif.

X-Ray Diagnosis and Therapy in Arthritis. M. F. Godfrey. California Med. **69:** 16–18, July 1948.

Four types of arthritis are commonly observed by the clinician: (1) osteoarthritis (degenerative or hypertrophic type); (2) rheumatoid arthritis (atrophic or proliferative); gouty arthritis; non-articular or soft-tissue rheumatism.

In osteoarthritis involving the interphalangeal joints the roentgenogram reveals narrowing of the cartilages and a broadening of the articular ends of the bones, which show a tendency toward proliferative changes at the periphery of the articular surfaces. In more advanced stages there may be a "hill-and-valley" grooving of the badly worn ends of the bones.

In rheumatoid arthritis involving the hands, there is destruction of the cartilages of the proximal joints of the fingers, the metacarpal-phalangeal joints, and the carpal regions, with fusiform swelling about the proximal joints of the fingers. The distal joints of the fingers are uninvolved. No new bone is laid down about the joints. If the spine is involved, the extremities are usually spared, and vice versa. In some cases the first evidence of disease in the back is in the sacroiliac joints, manifest roentgenographically as a loss of sharp definition of the outlines of the articular surfaces of one or both joints. Eventually actual bony ankylosis occurs.

Gouty arthritis may show no bone changes roentgenographically even in the late stages. When roentgen signs are present, they consist in definite punched-out areas in the subchondral bone at the heads or bases of the long bones of the hands or feet. Destruction of the articular surfaces of one or many joints may eventually take place.

Non-articular or soft-tissue rheumatism may cause roughening of the periosteum of the long bones and is associated frequently with capsulitis, pericapsulitis, and tendon sheath inflammation.

Roentgen therapy may be given locally over inflamed joints, for relief of pain, in osteoarthritis, rheumatoid arthritis, gouty arthritis, and in cases of capsulitis, pericapsulitis, bursitis, or tendinitis. It appears to relieve muscle spasm as well as to improve circulation and lymphocytic infiltration, but it does not deter degeneration of the joint. The author's technic is briefly as follows: For the elbow, wrist, ankle, shoulder, hip, and knee, the dose is 100 to 150 r per treatment. Treatments are given twice weekly, two ports, anterior and posterior, being employed for the larger joints. Four to eight treatments are given. A second course of four treatments may be given after an interval of six to twelve weeks.

For spondylitis, radiation is given along the entire spine, by segments, ports 10 cm. in width being used. Not more than half the spine is irradiated at one sitting. A dose of 75 r is given to each field twice weekly for three weeks. The course may be repeated after suitable intervals, but not more than 1,000 r is given to any one field.

For bursitis four treatments given daily or at two-day intervals usually relieve spasm and pain. It is well in these cases to obtain a roentgenogram of the joint before therapy to rule out fracture or metastatic bone lesion.

MAURICE D. SACHS, M.D.
Cleveland, Ohio

Bone and Joint Changes in Hemophilia, with Report of Cases of So-Called Hemophilic Pseudotumor. Ralph K. Ghormley and Reed S. Clegg. J. Bone & Joint Surg. **30 A:** 589–600, July 1948.

Of 150 patients with hemophilia seen at the Mayo Clinic, 76 were sufficiently severe for definite diagnosis, and of these, 44 or 58 per cent showed pathological changes in the bones and joints. All these patients were males; their average age was 17.3 years. The knee was most frequently involved, followed by the ankle, elbow, hip, wrist, patella, and phalanx in that order.

Earlier contributions on the subject are reviewed and six case reports are added to the literature. These six patients presented pseudotumors which seemed to be the result of hemorrhage into the soft tissue with subsequent erosion and destruction of the underlying bone, sinus formation, secondary infection, and terminal hemorrhage or infection.

No definite description of the bone lesions is given, possibly due to the lack of uniformity of the process. The authors state that it is difficult in a given case to determine whether the hematoma extends from hemorrhage in a neighboring joint or whether the hemorrhage is subperiosteal or intramedullary in origin.

Twenty illustrations, including 13 roentgenograms; 2 tables.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Aseptic Necrosis in Gaucher's Disease. Alvin M. Arkin and Albert J. Schein. J. Bone & Joint Surg. **30 A:** 631–641, July 1948.

The purpose of this paper is to draw attention to the observation that aseptic necrosis of bone is a very significant factor in Gaucher's disease of bone.

Six case reports and the corresponding roentgenograms are presented, showing the involvement of the femoral capital epiphysis, with changes similar to Legg-Perthes disease, in patients who were known to have Gaucher's disease. Some of these patients also present dense linear markings in the bone structure, similar to that seen in caisson disease.

The characteristic bone lesion of Gaucher's disease is a radiolucent and rarefied area of bone, due to infiltration of Gaucher cells. The increased density in the bone as here presented is believed due to the infiltration of the cells around the small arteries and capillaries, sufficient to cut off circulation and produce aseptic necrosis.

Seventeen roentgenograms.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Coexisting Multiple Myeloma and Paget's Disease of Bone Treated with Stilbamidine. Carl Reich and Alexander E. Brodsky. J. Bone & Joint Surg. **30A:** 642–646, July 1948.

A 52-year-old white male had been treated for four years for pain in the back and hips. Roentgen examination showed diffuse osteoporosis of the thoracolumbar spine with ballooning of the intervertebral disks and wedging and compression of the fourth, sixth, seventh, and eighth thoracic vertebrae. The upper portion of the left femur showed characteristic Paget's disease of the bone; the upper right femur, moderately large decalcified areas without adjacent sclerosis. The upper portions of both humeri and the ribs showed punctate decalcification. Urine examination for Bence-Jones protein was negative. In spite of this latter observation, the possibility of multiple myeloma was considered, and further laboratory tests were undertaken, showing hyperglobulinemia with high total serum protein and serum globulin. Sternal puncture definitely established a diagnosis of multiple myeloma.

This is believed to be the first reported case of Paget's disease complicated by multiple myeloma of the bone. The suggestion is offered that this combination may be more frequent than is realized, and that, in the presence of decalcification accompanying Paget's disease, bone marrow study should be performed.

The authors discuss the use of stilbamidine to relieve the pain and discomfort of the multiple myeloma. In this case definite relief was obtained and the patient returned to gainful occupation. No curative effect of the drug has been claimed.

Two roentgenograms; 1 photomicrograph.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Fracture-Dislocation of the Hip Joint: Nature of the Traumatic Lesion, Treatment, Late Complications, and End Results. Marshall E. Urist. J. Bone & Joint Surg. **30A:** 699–727, July 1948.

This is the third, and last, of a series on injuries of the hip (for the others see Am. J. Surg. **74:** 586, 1947, and Ann. Surg. **127:** 1150, 1948. Absts. in Radiology **51:** 442, 1948, and **52:** 765, 1949). It reports 27 cases of hip dislocation associated with major fractures of the acetabulum or femoral head. These include 15 cases of posterior dislocation with fracture of the posterior rim of the acetabulum, 8 fracture dislocations irreducible by closed manipulation, and 4 instances of posterior dislocation with fracture of the head of the femur.

The nature of the injury to the joint was studied in 15 cases treated by open operation. The major damage was sustained by the acetabulum, the periarticular ligaments, tendons, muscles, the ligamentum teres, and the retinacula of the joint. The extent of injury to the acetabulum varied from small chip fractures to involvement of a large segment of the acetabular rim. It was observed that small fragments could come to rest between the articular surfaces and injure them, while large fragments were usually displaced and on replacement would, as a rule, survive. The major damage to the soft parts of the joint was usually sustained by the external portion of the capsule. There was almost always some damage to the femoral head, with separation of the head or a circular depression, either of which may be overlooked on the roentgenogram. The ligamentum teres could not always be inspected in these studies but was found to be stretched and frayed in some instances. Blood clot and organized hemorrhage were seen in the retinacula in two cases. The significance of this finding was not noted until later, when both patients showed aseptic necrosis of the femoral head. The retinacula, three flattened bands of loose fibrous connective tissue containing blood vessels, lie partly within and partly outside the reflected capsule on the inferior, posteroinferior, and posterosuperior aspects of the joint. They carry the blood supply to the femoral head from branches of the medial femoral circumflex vessels. Their role in aseptic necrosis of the hip deserves further study.

In the 15 cases with fracture of the rim of the acetabulum, the diagnosis of fracture was not recorded in about 25 per cent, and in several other cases extensive fractures were not appreciated by the surgeons who administered emergency treatment and manipulated the dislocation. The oversight is easily understood. Unless one knows intimately the roentgen appearance of the hip joint, the fracture may seem to be obscured by the head of the femur in films taken before reduction. In cases in which the fracture was finally noted in the post-reduction films, a false idea of the apposition of the fracture lines was sometimes conveyed by examination of only the anteroposterior view of the hip. A true picture of the displacement of the rim fragments is best obtained in a postero-oblique view, with the injured side

elevated 60 degrees, the patient lying supine on the cassette, thus placing the posterior portion of the acetabulum in profile.

In the 8 cases in which the dislocated hip could not be reduced by closed manipulation, the difficulty was due either to a comminuted fracture of the acetabulum with intra-articular displacement of fragments, or to extensive fracture of the entire acetabulum with disorganization of the joint cavity. Stereoscopic roentgenograms were useful in demonstrating the bone fragments and distortion of the joint cavity in these cases.

Gross fractures of the head of the femur are considered rare in dislocation of the hip. As stated above, there were but 4 cases in this series.

Among the complications of fracture-dislocations of the hip, retroperitoneal hemorrhage may occur in comminuted fractures of the acetabulum where the blood is extruded internally beneath the parietal peritoneum. Distention, vomiting, and fever following the injury should lead one to suspect this condition.

Irritation, obstruction, or laceration of the urethra occurred in several cases in this series and thrombophlebitis was seen once. Thrombosis of the hemorrhoidal veins may occur. Sciatic neuritis occurred, possibly from stretching or irritation of the nerve by the acetabular fragment or the femoral head. Sciatic nerve injury is quite a potentiality, the peroneal portion of this nerve being apparently more susceptible to injury than any other. When there is an indication of sciatic nerve injury with dislocation and fracture, it is thought that open reduction should be resorted to.

Avascular necrosis of the head of the femur was seen in two patients. A review of the operative notes on these patients suggests that this complication is associated with thrombosis of either the retinaculum or the intertrochanteric branches of the medial femoral circumflex vessels. The change occurs between six and eighteen months after injury and the absence of weight-bearing does not seem to prevent injury to the femoral head.

Traumatic arthritis developed in 12 cases within a period of two years after injury. There were irregularities in the articular surface opposite the defect on the injured side of the joint. Eventual loss of joint space occurred in several patients.

The treatment of fracture-dislocation of the hip is thoroughly considered.

Thirty-nine illustrations, including 31 roentgenograms; 4 tables. JOHN B. MCANENY, M.D.
Johnstown, Penna.

Coxa Plana. M. Beckett Howorth. J. Bone & Joint Surg. **30A:** 601–620, July 1948.

Coxa plana, known also as Legg-Perthes disease, Calvé's disease, osteochondritis deformans juvenilis, and (though inaccurately) as aseptic necrosis of the upper femoral epiphysis, is more common in boys than in girls and in about 90 per cent of the cases is unilateral. The disease is fundamentally a vascular disturbance, followed by degenerative changes in the femoral head. The soft tissues about the joint become swollen, edematous and hyperemic, especially the synovial membrane. Perivascular lymphocytic and plasma-cell infiltration are commonly found. There is softening of the diaphyseal side of the disk with decalcification. Later there are absorption and reformation of bone. The capital epiphysis is deformed and there is subluxation of the hip followed by deformity of the acetabular surface.

In the first stages of the disease, lasting several weeks, there is only soft-tissue change with synovitis. Next comes the degenerative or active stage, lasting two years. This is followed by the healing stage, extending over three or four years, and finally the residual stage, with deformity.

The most common symptom is a slight limp with pain referred to the groin and the middle aspect of the thigh or the knee, made worse with use. The symptoms usually increase in severity with the advance of the disease until the end stage, when the disability is due to faulty mechanics.

Roentgenographically, the first change noticed is a globular swelling of the capsule with subluxation of the femoral head laterally. There is no change in the shape of the articular cartilage as yet. Later on, there is decalcification on the diaphyseal side of the epiphysis followed by a dense irregular area in the capital epiphysis. The head subsequently becomes decalcified and flattened. The neck becomes thicker and shorter. Still later, the decalcified areas become recalcified and the trabeculation reappears, but the head is flattened and remains subluxated. In middle life, osteo-arthritic changes often develop, due to faulty mechanics.

The treatment consists essentially in prolonged rest of the affected joint, but numerous operative procedures have been used of late.

Fifty roentgenograms; 4 photomicrographs.
JOHN B. MCANENY, M.D.
Johnstown, Penna.

Laminagraphy Through Plaster Casts in Postreduction Roentgenography of Congenitally Dislocated Hips. Bernard S. Epstein. J. Bone & Joint Surg. **30A:** 778–780, July 1948.

This short presentation suggests the use of laminagraphy to determine the exact status of bone structures in patients being treated for congenital dislocation of the hip, who are fixed in plaster. The authors use a Kieffer laminagraph with a spiral motion, 150 ma.-seconds, 55 to 60 kv., 30 inches distance, and par-speed screens. This procedure is said to define the bone structures better than the usual procedure of over-exposed Bucky films and to give more information as to the status of the bone structure.

Two roentgenograms. JOHN B. MCANENY, M.D.
Johnstown, Penna.

Fractures of the Talus. Barnard Kleiger. J. Bone & Joint Surg. **30A:** 735–744, July 1948.

This is a review of 29 cases of fresh fracture of the talus. In 11 simple linear fractures through the body, close to its juncture with the neck, the results were uniformly good with immobilization. In 2 cases complicated by additional fractures the outcome was not as good.

The medial articular surface was fractured once, the lateral articular surface five times, and the posterior tubercle twice in this series. If these fractures were uncomplicated by other injuries, the result was good. Where a fragment of bone is displaced from the superior articular surfaces, the prognosis is not necessarily poor, if the fragment can be manipulated into its proper position. It is believed that fractures of the articular surface should be reduced either by closed reduction or by operation and the fragment left in place, in which case adequate healing usually occurs.

In 8 patients, the fracture was through the body near its juncture with the neck, with displacement. If the displaced fragment could be reduced accurately, union usually took place. The only exception was when the proximal fragment was displaced posteriorly, tearing the ligaments and depriving the capital fragment of its normal blood supply. In these cases, the result was always bad and aseptic necrosis was likely to develop. It was thought that arthrodesis of the ankle joint might well have been done as a primary procedure in these latter conditions.

Thirty-three roentgenograms.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Myxochondrosarcoma of the Talus. H. Paul Longstreth, Pio Blanco, and Samuel Sanes. J. Bone & Joint Surg. **30A:** 774–778, July 1948.

This is a detailed case report of a 62-year-old white male who had a minor injury to his right ankle, followed by limitation of motion and tumor formation along the dorsum of the foot over the talus. Roentgen examination showed destruction of the superior border of the talus with invasion of the overlying soft tissue. A biopsy was done, establishing the diagnosis of chondrosarcoma. Roentgen therapy was administered for a total of 5,700 r to the right foot, in two courses. About one year later, examination showed no essential change in the bone. The patient then submitted to amputation of the lower right leg. Examination of the amputated member showed a definite myxochondrosarcoma. Five months later, an area of increased density was apparent in the right apical region of the chest, accompanied by cavity formation. Tuberculosis was suspected, but apparently not metastasis. Shortly afterward, the patient committed suicide. Autopsy showed metastatic myxochondrosarcoma in the right lung.

This is the eleventh case of myxochondrosarcoma of the talus to be reported. The age is between eleven and sixty-two years, with 8 male patients and 3 females. No definite relationship between injury and tumor formation has been established. Amputation is thought to be the best treatment. The differential diagnosis between myxochondrosarcoma and osteogenic sarcoma, myeloid sarcoma, giant-cell tumor, and fusiform-cell sarcoma must be made. Chondrosarcoma grows slowly, as shown in the present case report, in which there was a lapse of three and one-half years from the onset of symptoms to the time of death.

Six illustrations, including 1 roentgenogram.

JOHN B. MCANENY, M.D.
Johnstown, Penna.

Bilateral Osteochondritis of the Tarsal Navicular and the First Cuneiform. A Case Report. Arch F. O'Donoghue, Edmund S. Donohue, and Wayne W. Zimmerman. J. Bone & Joint Surg. **30A:** 780–781, July 1948.

While osteochondritis has been found in most of the bones of the body, bilateral involvement of the tarsal navicular and first cuneiform has seldom been recorded. In the case reported here roentgenographic examination of a three-year-old boy showed that the first cuneiform of each foot had a fragmented, moth-eaten appearance. A year later both tarsal naviculars—not yet completely ossified—showed evidence of fragmentation. Treatment was by supportive plates.

Two roentgenograms.

THE GENITO-URINARY SYSTEM

Value of Urography in Elucidation of Nonurologic Complaints. Allan K. Swersie. New York State J. Med. **48:** 1607–1609, July 15, 1948.

Gastro-intestinal symptoms are often prominent in disease of the upper urinary tract. Because of this, urographic studies should be done if gastro-intestinal films show nothing to account for such complaints. Two examples illustrate this point. In one case "gall-bladder symptoms" proved to be the result of a mild right hydronephrosis due to constriction at the uteropelvic junction. The second patient gave a history of epigastric pain attributed to ulcer, in spite of negative x-ray studies. He was found to have a crossed ectopia with probable fusion of the kidneys. Following passage of a calculus he was relieved of all complaints.

A third patient had urinary complaints and urography showed an extrinsic mass exerting pressure on the bladder. This proved to be an ovarian cyst. This case is thus the exact opposite of the others, an example of non-urologic disease producing urologic findings.

Three roentgenograms. ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Pyelography as an Aid to the Differential Diagnosis of Upper Abdominal Masses. Charles Eberhart and Donald E. Beard. J. M. Assoc. Georgia **37:** 265–269, July 1948.

Routine retrograde and intravenous pyelography are useful aids in the diagnosis of upper abdominal masses. The authors stress, in particular, the value of lateral and respiratory pyelography.

The lateral pyelogram made with the affected side toward the film under normal conditions discloses the renal pelvis and calices superimposed on the bodies of the 12th thoracic and 1st and 2nd lumbar vertebrae. The kidney occupies a vertical position. In the presence of renal, extraperitoneal, and intraperitoneal masses, the kidney may be displaced or rotated to the point of diagnostic importance. Differentiation of pelvic renal calculi, parenchymal calcification, gallstones, and stones in the common duct may be made with this technic. The lateral projection is also useful in the diagnosis of renal tumors and cysts, primary retroperitoneal tumors, and retroperitoneal infection. Retroperitoneal tumors may produce torsion but never cause deformity of the caliceal structures. If the kidney is rotated on two or more axes the lesion is likely to be intrarenal. Metastatic disease and tumors and cysts of the pancreas also rotate or displace the kidneys.

Respiratory pyelography is employed most advantageously in the diagnosis of perirenal disease. Fixation of a kidney may, however, be more apparent than real when the diaphragm is fixed by subphrenic disease.

The text of this paper is largely a review of the literature. The authors' own experience is presented in the form of roentgenograms with brief case histories.

Eight roentgenograms. LOUIS BERNSTEIN, M.D.
Hartford, Conn.

Roentgen Diagnosis of Tumors of the Urinary Tract. Paul C. Swenson, and Francis F. Hart. Pennsylvania M. J. **51:** 1114–1121, July 1948.

The purpose of this paper, as stated by the authors, is to correlate the gross pathologic changes found in

urinary tract tumors with the findings on x-ray examination. Plain films of the genito-urinary tract, intravenous pyelograms, and retrograde pyelography are employed in diagnosis. For excretory urograms, 20 c.c. of diodrast or of neo-iopax is routinely given. The patient is questioned as to a history of allergy and the first cubic centimeter is administered very slowly. Adrenalin is kept ready for immediate use at all times. For retrograde pyelograms, 15 per cent skiodan is used.

Simple cysts rarely deform the calices unless they are very large. They are unilateral and appear as a homogeneous soft-tissue shadow with a smooth outline.

In polycystic disease the kidneys appear to be normal until the cysts become large. The affection is both congenital and familial, and the family history, together with bilateral deformities, should suggest the diagnosis.

Benign and malignant tumors of the parenchyma in the adult cannot be differentiated radiographically. One usually sees a rather huge mass deforming the upper or lower pole of the kidney, with the classical symptoms of pain and hematuria. One third of all renal tumors show calcific deposits on x-ray examination. This finding is misleading, however, because there are so many other causes of calcification. Hemorrhage into the kidney pelvis with a resultant clot will produce bizarre pictures on both intravenous and retrograde urography, and a tumor which has become so large that it displaces or rotates the kidney, usually elongates the calices and deforms the pelvis to further distort the x-ray findings.

Benign and malignant tumors of the renal pelvis cannot be differentiated by x-ray. The papillomas and papillary endotheliomas deform the renal pelvis by their growth. The alveolar carcinomas and squamous-cell carcinomas infiltrate and cause little deformity. They metastasize early to almost every organ.

Wilms' tumor comprises 20 per cent of all malignant tumors in children. It is almost always evident clinically by the presence of a painless mass in the upper abdomen in the young child. A pyelogram will show a shift of the kidney and deformity of the pelvis due to pressure.

Primary tumors of the ureters are rare, but secondary tumors, as a result of seeding from papillary tumors of the renal pelvis, are comparatively common. The diagnosis of these tumors is difficult because such conditions as ureteritis cystica, hydronephrosis, pyonephrosis, and blood clots deform the ureters and produce a similar picture.

Bladder tumors are sometimes found in double contrast examinations or in cystograms, but can usually be better visualized by cystoscopy.

Seven roentgenograms. JOSEPH T. DANZER, M.D.
Oil City, Penna.

Roentgen Diagnosis of Diffuse Leukemic Infiltration of the Kidneys in Children. John F. Gowdey and Edward B. D. Neuhauser. Am. J. Roentgenol. **60:** 13–21, July 1948.

Infiltration of the kidneys is frequently found postmortem in patients dying of leukemia (63 per cent of 123 cases reported by Kirshbaum and Preuss: Arch. Int. Med. **71:** 777, 1943). When leukemic kidneys are studied by excretory urography, the roentgen appearance is characteristic, but may be confused with that produced by polycystic kidneys. There may be extreme enlargement of the kidneys with elongation of the renal plevis, infundibula, and calices. Function is usually well preserved, and there are no rounded pressure defects. Three case reports are included, with accompanying roentgenograms and photomicrographs. In Case III, one of the kidneys infiltrated with leukemic deposits was given roentgen therapy and the opposite kidney used as a control. The kidneys were then checked by excretory urography. The treated kidney showed reduction in size five days after irradiation, evidently due to destruction of radiosensitive leukemic cells. It is suggested that when renal enlargement is detected roentgenographically by excretory urography, the diagnosis of leukemia may sometimes be inferred.

Five roentgenograms; 4 photomicrographs; 1 photograph. JAMES C. KATTERJOHN, M.D.
Indianapolis, Ind.

Diagnosis and Management of Ureteral Ectopia. Thomas D. Moore. J. Urol. **60:** 50–62, July 1948.

The author reports 5 cases of ureteral ectopia and reviews the symptomatology, diagnosis, and treatment, referring to several other cases reported in the literature. In the female, the ectopic ureteral orifice is found in the urethra, the vestibule, the vagina, or the uterus. Since all of these locations are distal to the vesical sphincter, urinary incontinence with constant dribbling is the usual presenting symptom. In the male, however, in whom the ectopic ureteral opening is most often found in a seminal vesicle, ejaculatory duct, or the posterior urethra, all of which are proximal to the external vesical sphincter, urinary leakage is not present and the presenting symptom complex is that of unexplained pyuria.

Embryologically, the ureter from the upper segment in renal duplication develops at a later date and is therefore the one usually showing an ectopic orifice. Pathologically, the most frequently encountered type of ureteral ectopia is a complete unilateral duplication of pelvis and ureter with an ectopic opening of the supernumerary ureter. Not infrequently, coexisting anomalies of the genital and urinary tracts are found. The ectopic orifice is often extremely small and difficult to visualize, with diffuse ureterectasis and pyelectasis above the narrowed terminal opening. Because of resulting urostasis, approximately 90 per cent of such cases show evidence of infection. The segment of kidney drained by the aberrant ureter may be hypoplastic or hydronephrotic.

In the author's opinion, intravenous pyelography provides the most important diagnostic aid, especially when the ectopic ureteral opening is demonstrated and can be subsequently catheterized. In retrograde pyelography, however, it must be borne in mind that the lower segment of a duplicated kidney can assume essentially the outline of a normal kidney. Careful inspection of possible sites of the ectopic orifice with a direct vision cystoscope is another important diagnostic procedure. The efficacy of the latter may be augmented by the intravenous administration of indigo carmine, which will subsequently appear at the ectopic orifice.

In treating a case of normally functioning kidney with a single ectopic ureter, it is aimed to conserve the kidney by transplantation of the aberrant ureter to the bladder if the ureterectasis does not contraindicate the procedure. If a marked degree of ureterectasis exists, a complete heminephro-ureterectomy or nephro-ureterectomy may be necessary, since conservative ligation of the ureter results in a high percentage of failures.

Heminephrectomy is the operation of choice in cases of duplication where the blood supply is not intricate; otherwise, complete nephrectomy may be necessary if there is a normal opposite kidney.

Six roentgenograms. PAUL W. HOFFERT, M.D.
University of Pennsylvania

Recognition and Surgical Correction of Retrocaval Ureter: A Case Report. C. D. Creevy. J. Urol. **60:** 26–30, July 1948.

Thirty-eight cases of retrocaval ureter have been reported in the literature. Approximately half of the cases are asymptomatic and the other half cause symptoms of obstruction and hydronephrosis.

Retrocaval ureter is an anomaly of the venous system in which the vena cava is formed from veins that lie anterior to the ureter in the embryo, and which normally disappear early in the course of development. The ureter thus passes behind the vena cava a short distance below the renal pelvis. Its aberration in course is characteristic and readily identifiable on a pyeloureterogram.

A case is reported with preoperative diagnosis and successful correction.

Four roentgenograms. VERN W. RITTER, M.D.
University of Pennsylvania

THE BLOOD VESSELS

Diagnosis and Treatment of Arteriovenous Aneurysms in the Vicinity of the Cerebral Hemispheres. G. Weber. Schweiz. med. Wchnschr. **78:** 629–634, July 3, 1948. (In German)

This report covers 15 cases of arteriovenous aneurysm of the cerebrum, all demonstrated by arteriography. This condition is a congenital anomaly rather than a true tumor. Clinically the patients fell into several groups. Four patients had epileptiform seizures; 4 showed the residua of subarachnoid hemorrhage with or without a hemiparesis; 6 had signs of both subarachnoid hemorrhage and epileptiform seizures. One patient, a girl of nine, had monthly migraine accompanied by nausea and vomiting, with a slowly progressive left hemiparesis.

The symptoms of headache, vomiting, and dizziness have been described as typical of intermittent elevation of the intracranial pressure, and in arteriovenous aneurysm they are usually accompanied by jacksonian attacks, and almost always by hemiparesis. In 14 of these patients the symptoms began between the eighth and twenty-eighth years; in one the onset was at thirty-six years. Onset in later life, however, is not extremely uncommon. The conclusive proof of the diagnosis in each of the author's patients was obtained by cerebral arteriography, and some fair reproductions of a selection from these arteriograms accompany the paper.

Treatment is of three types; direct exposure with radical extirpation, ligature of the homolateral internal carotid artery, and irradiation. One of the author's patients, was not treated and his subsequent course is not known. One was treated by extirpation, and recovered, but with occasional residual attacks; one had x-ray therapy only (8,000 r), with no relief from his attacks, but no progress of the disease and full working ability. The other 12 had carotid ligation, and in 10 x-ray therapy—from 2,400 to 8,140 r—was given in addition. In only one of these was there a slight and transitory hemiparesis as a result of treatment, and none became unconscious, somnolent, or aphasic. Preexisting hemiparesis was not greatly changed by the ligature. One patient showed a slight psycho-organic injury as a result of this treatment. Of the 12, one died of intercurrent pneumonia after three months; the others showed a lessened tendency to subarachnoid hemorrhage, especially after irradiation; seizures were lessened in number, but the use of phenobarbital makes this finding hard to evaluate.

Of the types of therapy available, extirpation has the advantage of complete cure of the lesion, but the associated damage will be maximum. The combination of ligature and irradiation does not produce as perfect results, but does less damage to the surrounding brain tissues. Individualization of treatment is essential, but the author inclines to favor ligation plus irradiation in most cases.

Four roentgenograms; 1 table.

LEWIS G. JACOBS, M.D.
Oakland, Calif.

RADIOTHERAPY

Roentgen Treatment of Extensive Epithelioma of the Larynx. Results in 139 Cases. Arthur U. Desjardins, Frederick A. Figi, and Luther M. Vaughan. Am. J. Roentgenol. **60:** 29–36, July 1948.

"To practice medicine means not only to try to cure patients when this is feasible, but also to relieve suffering in any form when a cure is impossible." With this premise in mind, the authors treated 139 patients with extensive and advanced laryngeal epitheliomata from 1936 through 1945. They used 200-kv. roentgen therapy, Thoraeus filter, and a target-skin distance of 50 cm. Two portals were employed (one directed to each side of the larynx) except in very large lesions, for which the number was increased to three (two on the most extensively involved side). The patients were treated daily (except Sunday) with 200–400 r to one portal. After trial and error it was found that the optimum dose was 3,500 to 4,000 r to each of two fields. The fields were larger (18 × 12 to 12 × 18 cm.) than customarily used by most therapists, but they had to be large to include all of the bulky lesions which were treated.

A very high degree of palliation was obtained in almost all of the cases in this series, and 12 of 71 patients treated up to 1942 were alive for periods of five to eleven years—a five-year survival rate (not cure rate) of 17. per cent, despite the fact that all had such advanced disease that surgery was not feasible. In the authors' words: "... indeed, a more unfavorable group of cases would be hard to find."

In discussing this paper, Dr. Douglas Quick states: "Such results demand, for irradiation, a trial in the less advanced cases; and for the more favorable and earlier cases they demand at least a consideration of radiation on an equal basis with surgery." Certainly the authors clearly demonstrate by this excellent paper that one cannot discount the importance of irradiation in the management of carcinoma of the larynx.

One table. JAMES C. KATTERJOHN, M.D.
Indianapolis, Ind.

Late Results of Radium Therapy for Carcinoma of the Uterine Cervix. Harry H. Bowing and Robert E. Fricke. J. A. M. A. **137:** 935–941, July 10, 1948.

Thirty-two years of experience are reflected in this report of 2,246 patients with carcinoma of the cervix treated with radium and roentgen therapy. Various factors are evaluated, such as age, extent of the primary lesion, and previous treatment, and an attempt to formulate a basis for prognosis is considered. The prognosis for the patient under forty-nine years of age is not as good as that for older patients. The most important factor is the stage of the disease. The more localized it is, the better the prognosis.

The authors justly emphasize the necessity for evaluation of each patient and for close observation and follow-up. Of their patients traced five years after leaving the hospital, 33 per cent were living.

Seven tables.

PAUL W. ROMAN, M.D.
Baltimore, Md.

Krukenberg Tumor with Osteoplastic Metastases. Joseph H. Zeigerman. Am. J. Obst. & Gynec. **56:** 187–190, July 1948.

This concise informative article describes a case of ovarian carcinoma with bone metastases of a predominantly osteoplastic nature. Previous reported cases describe the opposite picture of bone pathology, namely osteoclasia.

A 27-year-old woman complained of vaginal bleeding and of a mass in the abdomen. A salpingo-oophorectomy for a right ovarian tumor had been performed one year previously, but the exact nature of the tumor was not determined. A second operation revealed an ovarian tumor representing mucoid carcinoma of the Krukenberg type. Studies of the gastrointestinal tract were negative. Three courses of irradiation therapy were proposed, but shortly after the first course an x-ray survey of the entire skeleton, prompted by pain in the dorsolumbar spine and the thighs, revealed widespread osteoplasia of varying degrees. The patient died three months after the onset of the metastatic bone symptoms and eight months after the second operation.

No cause for the predominant osteoplasia is given; however, the author considers the possibility of a hormonal relationship, since estrogens may cause a deposition of calcium in the secondary trabeculae of the bone.

Two roentgenograms; 1 photomicrograph.

ROBERT H. LEAMING, M.D.
Jefferson Medical College

Wilms' Tumor. William J. Daw. J. Urol. **60:** 18–25, July 1948.

The author reviews 7 cases of Wilms' tumor seen at the Wilkes-Barre (Penna.) General Hospital from 1937 to 1945. Of these, 2 were first seen after the development of multiple metastases. In the other 5 cases nephrectomy was done and 3 of the patients have survived six, five and two years, respectively. Of these, 1 had preoperative roentgen therapy and all had postoperative irradiation.

The author feels that early nephrectomy, either transperitoneal or lumbar, followed by adequate roentgen therapy is the treatment of choice.

Eleven illustrations, including 3 roentgenograms.

JOHN O. LAFFERTY, M.D.
University of Pennsylvania

Treatment of Bladder Tumors. Archie L. Dean. J. Urol. **60:** 92–97, July 1948.

The author has analyzed and classified bladder tumors according to the best method of treatment under the following headings: (1) transurethral electrocoagulation; (2) transurethral implantation of radon seeds with or without electrocoagulation; (3) segmental resection of bladder wall; (4) suprapubic cystotomy with implantation of radon seeds with or without electrocoagulation; (5) uretero-intestinal anastomosis with removal of bladder and prostate; (6) cutaneous ureterostomy with removal of bladder and prostate; (7) roentgen therapy.

The therapeutic indications are summarized in seven tables, of which those having to do with irradiation are reproduced here, though the article is well worth reading in its entirety.

Transurethral Implantation of Radon Seeds With or Without Electrocoagulation

Single papillomas or single papillary carcinomas

1. Favorably situated as regards
   (*a*) Complete cystoscopic vision
   (*b*) More than 1.5 cm. from ureteral orifice
2. Not larger than 2.5 cm. base diameter. No infiltrating tumors.

Suprapubic Cystotomy with Implantation of Radon Seeds With or Without Electrocoagulation

A. Papillomas too large or unfavorably situated for transurethral treatment or segmental resection

B. Carcinomas (papillary or flat) no larger than 3 cm. in diameter

Tumors may touch trigone but must be at least 1.5 cm. from urethral orifice. These growths are not resectable and do not infiltrate the prostate

If radon seeds are placed within 1.5 cm. of a ureteral orifice, the ureter should be reimplanted in the bladder

Roentgen Therapy

A. Contact therapy for conditions better treated with radon seeds or resection

B. High-voltage and supervoltage (the latter preferable for tumors as deeply situated as those of the bladder)

For palliation in old, feeble patients with extensive anaplastic tumors and minimal ureteral obstruction

JOHN M. PHILLIPS, M.D.
University of Pennsylvania

Roentgen Therapy of Malignant Tumors of the Testis. Eugene T. Leddy. Am. J. Roentgenol. **60:** 39–44, July 1948.

The principles advocated by the author for the treatment of testicular tumors are based upon an experience with at least 500 cases in the past twenty years.

Biopsy should consist of simple orchiectomy without preoperative irradiation. Tissue examination will then reveal one of the following types of lesion: (1) teratoma, (2) adenocarcinoma of the seminoma type, or (3) adenocarcinoma of the testis. Seminomas and teratomas constitute about 95 per cent of the total.

Irradiation of seminomas and their secondary deposits is best carried out with roentgen rays of moderate voltage (130 to 140 kv.) Intermediate voltage is used

because treatment must always be extensive, because it is believed that there is no difference in the effectiveness of this type of radiation and that generated at higher levels (200 to 250 kv.), and because less harm will be done to the patient if this type of treatment is used. Four anterior abdominal fields and four corresponding posterior fields are treated; the mediastinum and the left supraclavicular space are always treated. Each field receives about 540 r (total dose, in air); two fields are treated daily, depending on the patient's tolerance. A similar course of treatment is again given one month later, and if metastatic deposits have been present in the abdomen before operation, a third course is given after a lapse of two months. The blood count is carefully watched during treatment.

That the methods of treatment employed are satisfactory is confirmed by the statistical study of Cabot and Berkson, who reported a 71 per cent survival for patients with seminomas receiving roentgen therapy and a 58.8 per cent survival without roentgen therapy. [Cabot and Berkson's study (New England J. Med. **220:** 192, 1939. Abst. in Radiology **34:** 259, 1940) was based upon a series of cases seen at the Mayo Clinic up to 1937 and must, therefore, have included a considerable number of the cases upon which the present paper is based.] The relation of the results to the extent of the disease is not discussed. In general, however, it was found that for cases with no evidence of abdominal metastases at the time of irradiation the three-year survival rate was twice as high as in cases known to have secondary disease in the abdomen.

The symptoms of para-aortic lymph node involvement are: dull aching pain in the back, bloating, belching, fullness in the abdomen, and constipation. When a definite mass of lymph nodes cannot be palpated in the abdomen, vague resistance to the examiner's hand and tenderness on deep palpation are usually considered suggestive of metastatic disease. Metastases may also be detected by excretory urography and other forms of roentgenography. Following involvement of the para-aortic nodes, the left supraclavicular lymph nodes are involved, and later the peribronchial nodes.

Since it is well known that seminoma of the testis responds well to roentgen therapy, the therapeutic test can often be used with high accuracy to judge the nature of metastatic lesions when their histopathology is unknown.

Malignant teratomas do not respond very well to roentgen therapy in Leddy's experience. Since some tumors may be an admixture of seminoma and malignant teratoma, they may respond initially, but continue to grow after the more sensitive elements have been destroyed.

"For the treatment of seminomas, roentgen therapy has assumed a position of prime importance and has altered the prognosis from one of hopelessness to one of subdued optimism. This is quite different from the prognosis of malignant teratoma of the testis. . . no technique of treatment which we have used within the limits of safety has been more than temporarily effective in the treatment of metastatic lesions caused by malignant teratomas." JAMES C. KATTERJOHN, M.D.
Indianapolis, Ind.

Roentgenologic Treatment of Lymph Nodes and Spleen in Brill-Symmers Disease. Sidney Rubenfeld. J. A. M. A. **137:** 849–852, July 3, 1948.

This paper is based upon observations on 9 cases of giant follicular lymphadenopathy (Brill-Symmers disease) and 10 cases of polymorphous-cell sarcoma (of Symmers). Giant follicular lymphadenopathy may remain unchanged throughout life; it may undergo transformation into lymphosarcoma, lymphoid leukemia, Hodgkin's disease, reticulum-cell sarcoma, or it may develop into polymorphous-cell sarcoma.

Giant follicular hyperplasia has been mistaken clinically for Hodgkin's disease. Its histologic picture, however, is distinctive. There is numerical and dimensional hyperplasia of lymph follicles, consisting exclusively of small lymphocytes. The follicles may remain intact or may rupture and permit escape of their cell components into the substance of the nodes. In the latter event the disease is transformed into polymorphous-cell sarcoma.

The author's patients ranged in age from twelve to fifty-nine years. There were 5 females and 14 males. Enlarged lymph nodes were the outstanding feature. These varied from 1 to 3 cm. in diameter and presented no characteristics to distinguish them from the other lymphomas. Splenomegaly was present in 3 cases and in 1 the liver was enlarged. There was a persistent leukopenia in 4 patients.

Two-hundred-kilovolt roentgen therapy was used to treat the lymph nodes and spleen, with two noteworthy variations in response. The nodes in giant follicular lymphadenopathy receded or disappeared under doses of 800 to 1000 r (measured in air). The nodes in polymorphous-cell sarcoma regressed only after doses of 2,000 to 3,000 r and frequently showed a latent period of reaction in contrast to the rapid disappearance of the nodes in giant follicular lymphadenopathy.

Sixty-six per cent of patients with giant follicular lymphadenopathy and 60 per cent of those with polymorphous-cell sarcoma are apparently well five or more years after institution of treatment. The disease develops and progresses slowly and in its early phase is reversible or curable. When a dedifferentiated structural modification has occurred, the course is irreversible and the outcome is fatal.

Seven illustrations. H. R. ZATZKIN, M.D.
University of Michigan

RADIOACTIVE ISOTOPES

Study of Peripheral Vascular Disease with Radioactive Isotopes. Part I. Daniel C. Elkin, F. W. Cooper, Jr., R. H. Rohrer, W. B. Miller, Jr., Patrick C. Shea, Jr., and E. W. Dennis. Surg., Gynec. & Obst. **87:** 1–8, July 1948.

Two methods for the use of radioactive sodium 24 in the investigation of circulatory physiology of the extremities are compared and discussed.

One method consisted in the intravenous injection of radioactive sodium into the antecubital vein, with determination of the circulation time to the leg and to the foot; curves were obtained by plotting the counting rate of Geiger-Müller detectors against time. Variations in circulation time by this method were found to be so wide in normal individuals that results would be rendered valueless in the diagnosis of circulatory dis-

orders. A great many variables and uncontrollable factors are involved in the procedure.

The second method involved injection of radioactive sodium directly into muscle and recording its rate of removal. This was believed to permit an objective evaluation of the effective blood flow through the capillaries, for the removal of the sodium from the muscle depends upon the volume of blood flow. A linear expression of the removal rate of the sodium is obtained by plotting counts per minute against time on semilogarithmic paper. A numerical logarithmic expression "K" of the slope of the line is used for comparative studies. Such studies have been made in 115 individuals, and are to be reported at a later date.

An electromechanical apparatus was designed for automatically recording impulses received from four Geiger-Müller tubes simultaneously. The counts are translated by electronic circuits into currents which activate pens of mechanical recorders.

Three photographs; 3 charts.

ALLAN K. BRINEY, M.D.
University of Pennsylvania

Thyrotoxicosis Factitia (Alimentary Thyrotoxicosis): Its Differentiation from Spontaneous Thyrotoxicosis with the Aid of Radioactive Iodine. Bengt N. Skanse and Douglas S. Riggs. J. Endocrinol. **8:** 532–543, July 1948.

A case of secretly self-induced thyrotoxicosis (thyrotoxicosis factitia) is described, and a second case in which circumstantial evidence strongly favored the same diagnosis is also discussed. In both patients the clinical picture was indistinguishable from that of endogenous thyrotoxicosis. The differential diagnosis was facilitated by the use of tracer doses of radioactive iodine. In endogenous thyrotoxicosis the urinary excretion of radioactive iodine is low compared to that of euthyroid individuals. In thyrotoxicosis factitia the excretion of radioactive iodine is higher than normal. Since the serum protein-bound iodine is elevated independently of the source of iodine-containing hormone, this test is not contributory to the differential diagnosis. Other conditions which may produce the same condition of elevated serum protein-bound iodine and high excretion of radioactive iodine are discussed.

EFFECTS OF RADIATION

Basal Metabolism in Cancer Patients in Relation to Radiotherapy. D. Agostini and P. Lorenzini. Radiol. med. (Milan) **34:** 415–420, July 1948. (In Italian)

The authors studied the basal metabolic rate of 56 cancer patients before, during, and after radiation therapy. From their observations they conclude that the basal metabolism rate is elevated 15 to 25 per cent in cancer patients before any treatment is given and goes even higher during radiation therapy, especially with radium. After treatment, the basal metabolism rate remained elevated in 48 per cent of the patients, was normal in 32 per cent, and low in 20 per cent. The weight of the patients varied inversely as the basal metabolic rate.

Many breast cancers showed a decreased basal metabolism rate following treatment, probably because of radiation effect on the thyroid or upon the sympathetic chain.

One chart.

CESARE GIANTURCO, M.D.
Urbana, Ill.

Generalized X-Ray Exanthema (Report of a Case). H. Schreiber. Radiol. clin. **17:** 207–212, July 1948. (In English)

A woman of 40 was given postoperative irradiation to the left chest and axilla following a microscopic diagnosis of carcinoma simplex of the breast and a "wide excision of the mamillary region." She received 1,440 mg.hr. to a palpable node in the axilla (type of radium applicator not stated) followed by a series of roentgen treatments, with 1,000 r to the lateral, 1,200 r to the medial, and 200 r to the inferior part of the breast, and 1,200 r to the anterior and 1,600 r to the posterior axilla (200 kv., 4 ma., 0.5 mm. copper and 1.0 mm. aluminum filter, 10 × 15-cm. fields, 40 cm. focal skin distance, 200 r per treatment); 250 r additional were given to the scar (160 kv., 4 ma., 1.0 mm. aluminum filter, 40 cm. F.S.D.). This led to erythema and desquamation which two weeks following completion of the treatment was regressing. About three days after this, however, a dark red, painful area extending far beyond the treated area had appeared. The temperature was normal. Treatment with calcium and benadryl (on the supposition of an allergic reaction) was without effect, and the lesion progressed, finally involving an area on the left forearm not in continuity with the rest of the lesion. This rash was partly homogeneous, partly composed of macules with a tendency to coalesce. The general condition remained good. A leukopenia of 2,400 white blood cells was noted, but was believed to be due to the previous irradiation. At the beginning of treatment, the percentage of eosinophils was 7; at the height of the reaction, it was between 2 and 3. Bland local applications were used, and recovery eventually occurred. The diagnostic possibilities are considered at some length, with the conclusion that this represents a nonspecific generalized post-irradiation erythema.

Three drawings.

LEWIS G. JACOBS, M.D.
Oakland, Calif.

X-Ray Injuries: The Preventable Occupational Hazard. Shirley J. DeVoe and George M. Corney. New York State J. Med. **48:** 1601–1602, July 15, 1948.

The fundamental points in x-ray and radium protection are emphasized rather briefly in this article. Some things are not given the proper emphasis, *i.e.*, the discarding of old cracked gloves, the use of filters on the fluoroscopic tube, limitation of fluoroscopic time, the prime importance of distance in radium protection, etc. These are errors of omission, however, and since the things that are discussed involve every radiologist's daily life, it would be worth while to refresh one's memory by reading the article in the original.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

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